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Health-related quality of life in gout: a primary care-based mixed methods study

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Arthritis Research UK Primary Care Centre, Keele University

Declaration

My interest in gout has developed throughout my clinical training as a specialist registrar in rheumatology. I have taken time out of my clinical training program in Mersey deanery to pursue this PhD. My research training has been funded by the National Institute of Health Research (NIHR) School for Primary Care Research (SPCR) Doctoral fellowship.

This thesis is nested within a larger cohort study of Health Related Quality of Life in gout in primary care at the Arthritis Research UK Primary Care Centre, Keele University. The initial research idea and PhD proposal were developed by Dr Edward Roddy. However the subsequent PhD plans, conduct of the study, analysis and interpretation of the findings are my own. In the Health Related Quality of Life in gout study, I developed the research protocol, study documents, gained NHS Research and Development and Ethical approval, organized mailing of the questionnaire, designed the data entry database brief and conducted all data analyses independently. The day to day running of the study was supported by the administration team at the Arthritis Research UK Primary Care Centre, Keele University. The supervisory team have provided advice during the writing of the thesis and study statisticians have provided statistical support where needed.

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Abstract

Background: Gout is the most prevalent inflammatory arthritis (2.5%) and may affect Health Related Quality Of Life (HRQOL) through its disease features, associated co-morbid and socio-demographic characteristics.

Methods: A systematic review of HRQOL in gout and the instruments used to measure it was performed. 1805 eligible patients in primary care were mailed a questionnaire to ascertain self-reported HRQOL (measured using Health Assessment Questionnaire Disability Index (HAQ-DI), Short-Form 36 Physical Function subscale (PF-10) and Gout Impact Scale (GIS)), gout, co-morbid and socio-demographic characteristics. Univariate unadjusted (T-test and analysis of variance) and multivariate adjusted (linear regression models) associations between HRQOL and independent variables were examined. Focus group interviews of participants' perspectives towards gout and its treatments affecting HRQOL were conducted and thematic analysis performed.

Results: 22 studies in the systematic review identified poor physical HRQOL in those with gout and co-morbidities. Existing studies were limited by use of either generic or gout-specific HRQOL questionnaires and mostly secondary care settings. 1184 completed questionnaires were received (response 65.5%). On multivariate adjusted analysis, worse generic and gout-specific HRQOL was associated with higher attack frequency, history of oligo/polyarticular attacks, allopurinol, body pain, depression, alcohol consumption and age. HRQOL measured using the GIS only was associated with serum uric acid $>360\mu\text{mol/L}$ and currently having an attack and using the PF-10 and HAQ-DI only with female gender, stroke and angina. The key themes arising from the qualitative interviews were the impact of gout characteristics, misunderstanding of gout and lack of information from physicians.

Conclusions: HRQOL in gout is affected by disease severity, medical and psychological co-morbidities and socio-demographic characteristics. Urate-lowering treatment should be initiated

early to prevent disease progression. Co-morbidities should be screened for and treated alongside gout. Factors associated with HRQOL differ according to the instrument used and the choice of instrument will depend upon the objectives of future research studies.

Glossary of terms

Health Related Quality of Life	The influence of political, economical, spiritual and cultural factors on quality of life that is related to health status. Conceptualisations of HRQOL include physical, social and psychological health perceptions (Wilson, Cleary 1995)
Clinimetric properties	A methodological discipline focussing on the quality of clinical measurement. The quality of measurement depends upon the quality of the questionnaire as well as the performance of the actual measurements (Feinstein 1983)
Generic questionnaires	These include health profiles and utility measures. Health profiles can address a variety of areas and can be used in any population regardless of the disease. Utility measures provide a single number as an indicator of the impact on quality and quantity of life (Guyatt, Feeny et al. 1993). Generic questionnaires used in this study are the Physical Function-10 and Health Assessment Questionnaire Disability Index.
Gout-specific questionnaire	The Gout Impact Scale focuses on aspects of health status that are of interest in gout only. In addition to being more responsive to change in gout, it may relate closely to areas routinely examined by clinicians (Guyatt, Feeny et al. 1993).
Gout suppressants	Defined in the Medline and CINAHL databases Medical Subject Headings (MeSH) as allopurinol, colchicine, naproxen, indomethacin and uricosuric agents.
Medical record review	Computerised medical records of consenting participants were reviewed for prescriptions of colchicine and allopurinol, serum uric acid and tophi in the two years preceding the study.
Read Codes	Thesaurus of the most commonly used clinical terms in medicine, used to

record patient encounters in general practice (Stuart-Buttle, Read et al. 1996)

Abbreviations

NIHR	National Institute of Health Research
SPCR	School for Primary Care Research
UK	United Kingdom
NHS	National Health Service
HRQOL	Health Related Quality of Life
BMC	BioMed Central
EULAR	European League Against Rheumatism
PF-10	Physical Function 10
HAQ-DI	Health Assessment Questionnaire Disability Index
GIS	Gout Impact Scale
NOS	Newcastle Ottawa Scale
CASP	Critical Appraisal Skills Programme
BMI	Body Mass index
MTPJ	Metatarsophalangeal joint
BC	Before Christ
AD	After Death
CI	Confidence Interval
GPRD	General Practice Research Database
THIN	The Health Improvement Network
CPRD	Clinical Practice Research Database
USA	United States of America
NHANES	National Health and Nutrition Examination Survey
GP	General Practice
ICD-9	International Classification of Diseases 9
ARA	American Rheumatism Association
SUA	Serum Uric Acid
MSU	Monosodium Urate
OAT	Organic Anion Transporter
GWAS	Genome Wide Association Scanning
MTHFR	Methylene Tetrahydrofolate Reductase
GCKR	Glucokinase regulatory protein
MRFIT	Multiple Risk Factor Intervention Trial
RR	Relative Risk

VS.	Versus
RCT	Randomised Controlled Trial
ARIC	Arthrosclerosis Risk in Communities
HPFS	Health Professionals Follow-up Study
ATP	Adenosine triphosphate
AMP	Adenosine Monophosphate
OA	Osteoarthritis
OR	Odds Ratio
WHO-QOL	World Health Organisation Quality of Life Bref
BREF	
SF-36	Short Form 36
CVD	Cardiovascular Disease
CHD	Coronary Heart Disease
BCLHD	British Columbia Linked Health Database
ULT	Urate-Lowering Therapy
NSAID	Non-Steroidal Anti-Inflammatory Drug
COX	Cyclooxygenase
IL	Interleukin
FDA	Food and Drug Administration
QOL	Quality of Life
WHO	World Health Organisation
OMERACT	Outcome Measures in Rheumatology Clinical Trials
GAQ	Gout Assessment Questionnaire
SEM	Standard Error of Measurement
SDC	Smallest Detectable Change
MIC	Minimal Important Change
CINHAL	Cumulative Index to Nursing and Allied Health Literature
IRT	Item Response Model
DIF	Differential Item Functioning
PC	Priyanka Chandratre
LC	Lorna Clarson
COSMIN	Consensus-based standards for the selection of health measurement instruments
ICC	Interclass Correlation Coefficient

LOA	Limits Of Agreement
Guyatt's RR	Guyatt's Responsive Ratio
AUC	Area Under Curve
ES	Effect Size
NR	Not Recorded
BIPQ	Brief Illness Perception Questionnaire
AIMS	Arthritis Impact Measurement Scales
MOS	Medical Outcomes Survey
ACR	American College of Rheumatology
RR	Response Rate
CS	Cross-sectional
CHT	Cohort
MCS	Mental Component Score
PCS	Physical Component Score
DASH	Disability of the Arm, Shoulder and Hand
RP	Role Physical
RE	Role Emotional
JFL	Joint with Functional Limitations
MH	Mental Health
RA	Rheumatoid Arthritis
WMN PCRN	West Midlands Network Primary Care Research Network
PIS	Patient Information Sheet
ARUKPCC	Arthritis Research UK Primary Care Centre
TIA	Transient Ischaemic Attack
PHQ-9	Patient Health Questionnaire 9
GAD-7	Generalised Anxiety Disorder 7
IPQ-R	Revised Illness Perception Questionnaire
VAS	Visual Analogue Score
ADL	Activities of Daily Living
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders fourth edition
NHS	National Health Service
SPSS	Statistical Package for the Social Sciences
SOP	Standard Operating Procedure
RUG	Research User Group

REC	Research Ethics Committee
MRC	Medical Research Council
IRAS	Integrated Research Application System
MDI	Multiple Deprivation Indices
SD	Standard Deviation
IQR	Interquartile Range
CO	Concern Overall
MSE	Medication Side Effects
UTN	Unmet Treatment Need
WBDA	Wellbeing During Attack
CDA	Concern During Attack
BSR	British Society of Rheumatology
HADS	Hospital Anxiety And Depression Scale
ANOVA	Analysis of Variance
MRR	Medical Record Review
GABA	γ - Amino Butyric Acid
M	Male
F	Female
K	Keele

Publications and presentations arising from this thesis

Peer-reviewed publications

1. Chandratre P, Roddy E, Clarson L, Richardson J, Hider SL, Mallen CD. Health-related quality of life in gout: a systematic review. *Rheumatology (Oxford)*. 2013 Nov;52(11):2031-40 (appendix 1)
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Oral presentations

October 2014	Health Related Quality of Life in gout: a cross-sectional analysis. North West Rheumatology Society Meeting, Liverpool
July 2014	Health Related Quality of Life in gout: cross-sectional analysis from a prospective cohort study. Society for Academic Primary Care Conference, Edinburgh
July 2014	Gout - 'not something you brag about'. A qualitative study of health related quality of life in gout. Society for Academic Primary Care Conference, Edinburgh
March 2014	Cross-sectional study of HRQOL in gout. Midland Rheumatology Society, Derby
October 2012	Health Related Quality of Life in gout: A systematic Review. Midlands Rheumatology Society, Rugby
June 2012	Health Related Quality of Life in gout: Key findings from the systematic Review. Arthritis Research UK Crystal Workshop, Manchester

Poster presentations

National Institute for Health Research (NIHR) School for Primary Care Research fellows conference September 2014	Health Related Quality Of Life in gout: cross-sectional analysis from a prospective cohort study 'Gout: not something you brag about'. A qualitative study of HRQOL in gout
National Institute for Health Research (NIHR) 5 th Research Training Camp, July 2014, Ashridge Business school	Health Related Quality Of Life in gout: cross-sectional analysis from a prospective cohort study
EULAR June 2014, Paris	Health Related Quality Of Life in gout: cross-sectional analysis from a prospective cohort study
West Midlands Physicians Association May 2014	HRQOL in gout: cross-sectional analysis from a prospective cohort study
British Society for Rheumatology April 2014	'Gout: not something you brag about'. A qualitative study of HRQOL in gout
British Society for Rheumatology May 2013	HRQOL in gout: a systematic review
National Institute for Health Research (NIHR) School for Primary Care Research fellows conference September 2012	Health Related Quality of Life in gout: A prospective cohort study

Planned publications from this thesis

1. Chandratre P, Mallen CD, Muller S, Hider SL, Richardson J, Rome K and Roddy E. Health Related Quality of Life in gout: A cross-sectional study.
2. Chandratre P, Roddy E, Mallen CD, Hider SL, Liddle J and Richardson J. A qualitative study of HRQOL in gout using focus group interviews.

Planned publications associated with this thesis

1. Prior JA, Roddy E, Chandratre P, Muller S, Richardson J and Mallen CD. Gout characteristics associated with depression, but not anxiety, in primary care
2. Walsh CP, Prior JA, Chandratre P and Roddy E. Allopurinol use and the illness perceptions of gout patients in primary care
3. Roddy E, Muller S, Rome K, Chandratre P, Hider SL, Richardson J, Blagojevic-Bucknall M and Mallen CD. Foot problems in people with gout in primary care: baseline findings from a prospective cohort study

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1 The concept of Health Related Quality of Life in gout

1.1 Introduction

This chapter provides an overview of the historical and current understanding of gout before introducing the concept of Health Related Quality of Life (HRQOL) as an outcome measure for patients with gout. It also describes the importance and relevance of HRQOL in the context of gout in a primary care setting. Finally it addresses gout-associated factors that may have an impact on HRQOL.

1.2 The history of gout

The classical presentation of acute gout (excruciating pain, swelling and erythema affecting the 1st metatarsophalangeal joint (MTPJ)) was first recognised by the Egyptians in 2640 BC (Nuki, Simkin 2006) and described later in 400 BC by the Greeks as 'Podagra', from the word 'pous' meaning foot and 'agra' meaning seizure (Nybakken 1960). Gout was a term first coined by Randolphus of Bocking (domestic Chaplain to the Bishop of Chichester) in 1200 AD (Pillinger, Rosenthal et al. 2007). The word 'gout' is derived from 'gutta' a Latin word meaning to 'drop', as it was believed that when the equilibrium of the four humours (black bile, yellow bile, blood and phlegm) was disturbed (due to excess of one over the others), one of those humours would drop or flow into the joint causing symptoms of pain, swelling and redness (Nuki, Simkin 2006).

1.3 The epidemiology of gout

1.3.1 Prevalence and incidence of gout

Wide variations in the prevalence of gout may result from heterogeneity in published studies. There are marked differences in the way individual studies ascertain the diagnosis of gout (for

example, the gold standard of urate crystal identification largely carried out in secondary care or a purely clinical diagnosis made by generalists in primary care) and whether the data captures an attack of gout in the lifetime (cumulative prevalence) or within a specified time period (period prevalence) (Roddy, Zhang et al. 2007). However the overall trend is that gout has increased in prevalence when compared to the last decade - from 1.39% (95% CI 1.37 to 1.41) in 1999 and 2000- 2005 according to cohort studies in the UK general practice (Mikuls, Farrar et al. 2005a; Annemans, Spaepen et al. 2008) to 2.49% (95% CI 2.48% to 2.51%, per 1000 person years) in the period between 1997 and 2012 in a study using the Clinical Practice Research Database (CPRD) (Kuo, Doherty et al. 2013). A higher prevalence may be attributed to better identification of patients in the inter-critical period of gout by direct standardisation including age, gender and length of data contribution (Kuo, Doherty et al. 2013). By contrast, in New Zealand the prevalence of gout seems to be decreasing from 4.7% in 1990 – 1992 (Klemp, Stansfield et al. 1997) to 2.8% in 2009 (Winnard, Wright et al. 2012). Geographical variation within the UK (highest prevalence in the North East followed by Wales) and gout's predilection for males worldwide is demonstrated in Table 1-1. Gout also seems to have a predilection for those with Maori ethnicity (prevalence rates of 10.3% (Stamp, Wells et al. 2013) and 6.4% (Klemp, Stansfield et al. 1997) in Maori compared with 2.3% and 2.9% in non-Maori respectively).

In the UK General Practice Research Database (GPRD) study between 1990 and 1999, the incidence of gout was variable between 1.19 cases (95% CI 1.15 to 1.23) to 1.80 cases (95% CI 1.76 to 1.84) per 1000 patient-years (Mikuls, Farrar et al. 2005a). A mean annual incidence of 12.4 cases of gout per 1000 persons was reported in a retrospective study of routinely collected data by the Royal College of General Practitioners Weekly Returns Service (Elliot, Cross et al. 2009). Other more recent primary care database based studies (The Health Improvement Network (THIN) and CPRD) show a slightly higher incidence of gout in the UK - 2.68 (95% CI 2.65

to 2.72) per 1000 person years between 2000 to 2007 (Cea Soriano, Rothenbacher et al. 2011) and 1.77 (95% CI 1.73 to 1.81) per 1000 person years in between 1997 and 2012 (Kuo, Doherty et al. 2013)). The increasing prevalence and incidence of gout in the UK and elsewhere are shown in Table 1-1

Table 1-1: The worldwide prevalence and incidence of gout

Study	Year	Case ascertainment	Design	Prevalence	Incidence
UK					
Kuo, Doherty et al. 2013	2012	Unreported	CPRD	2.51% per 1000 person years (highest prevalence 3.11% north east and 2.98% Wales)	1.77 (95% CI 1.73 to 1.81) per 1000 person years (highest incidence north east 2.30% and Wales 2.20%)
Cea Soriano, Rothenbacher et al. 2011	2000- 2007	Unreported	UK general practice database		2.68 per 1000 person years
Elliot, Cross et al. 2009	2001 - 2007	Prescription of allopurinol and consultation	Royal college of General Practitioners	Annual prevalence 0.46%	
Annemans, Spaepen et al. 2008 ¹	2000- 2005	IMS disease analyser	GP records	1.4%	
Mikuls, Farrar et al. 2005a	1990 - 1999	Physician diagnosis and drug codes	GP database	1.4% (>7.5% in men aged > 65 years)	11.1 in 1990 to 18 per 10,000 patient years in 1994

¹ Study based in UK and Germany

Study	Year	Case ascertainment	Design	Prevalence	Incidence
New Zealand					
Stamp, Wells et al. 2013	-	Hyperuricaemia and gout in Maori and non-Maori people	Electoral roll	Gout - Maori 10.3%, non-Maori 2.3% Hyperuricaemia- Maori 17%, non-Maori 7.5%	
Winnard, Wright et al. 2012	2009	Prescription of colchicine or allopurinol or hospitalisation	National level health data sets	2.89% (adjusted for age, gender and ethnicity)	
Klemp, Stansfield et al. 1997	1990 - 1992	1977 ARA criteria for gout	Random selection from schools and electoral rolls	4.7% overall (Maori 6.4%, European 2.9%) Maori male to female 5:1, European male to female 8:1	
USA					
Krishnan, Chen 2013	1959-1962, 2009-2010	Self-reported gout	NHANES surveys	Unadjusted - 6/1000 to 26/1000. Adjusted prevalence rate ratio 1.86 (1.28, 2.71) men and 1.21 (0.81, 2.11) women	
Zhu, Pandya et al. 2011	2007 - 2008	Hyperuricaemia (>7 mg/dL for men and > 5.7 mg/dL for women)	NHANES	3.9% overall (2% females, 5.9% males)	
Bhole, de Vera et	1950 –	Women only	Framingham Heart		13.1 per 1000 person years

Study	Year	Case ascertainment	Design	Prevalence	Incidence
al. 2010	2002		study		for SUA 6-6.9 mg/dL and 27.3 per 1000 for SUA 7-7.9 mg/dL
Wallace, Riedel et al. 2004	1990 - 1999	ICD 9 codes for gout or prescription for gout	Administrative claims database	2.9/1000 in 1990 to 5.2/1000 in 1999 (in over 75 years of age, 21/1000 in 1990 to 41/1000 in 1999)	
Arromdee, Michet et al. 1999	1977- 1978 and 1995- 1996	1977 ARA criteria	Computerised medical records		45 per 100000 in 1977-78 62.3 per 100000 in 1995-96
Italy					
Trifiro, Morabito et al. 2013	2005- 2009	Hyperuricaemia (> 360 µmol/L) and gout defined using ICD 9 codes	Italian Primary care database	6.7/1000 in 2005 9.1/1000 in 2009	0.93 /1000 in 2005 and 0.95/1000 in 2009

Abbreviations: CPRD; Clinical Practice Research Database, ARA; American Rheumatology Association, NHANES; National Health and Nutrition Survey, ICD 9; International Classification of Diseases 9, GP; General Practice

1.3.2 Pathophysiology of gout

Gout is caused by excess uric acid, an insoluble end-product of primarily endogenous purine metabolism due to de novo synthesis and nucleic acid breakdown (600 mg per day) and a minority through exogenous dietary intake (100 mg per day) (Richards, Weinman 1996). High levels of serum uric acid lead to deposition of monosodium urate (MSU) crystals in and around joints and soft tissue once the physiological threshold for their saturation ($360 \mu\text{mol/L}$) is exceeded (Edwards 2008). A high level of uric acid (hyperuricaemia) can result from over production (10%) and renal underexcretion of purines (90%) (MacGregor, Silman 2003). Renal transport of urate has traditionally been thought to incorporate glomerular filtration, near complete reabsorption of the filtrate, secretion and post-secretory reabsorption in the proximal tubule (Roch-Ramel, Guisan 1999). Fractional excretion of the glomerular filtered urate is only 10% (Edwards 2008), with the rest being reabsorbed by renal urate transporters such as URAT1 (encoded by SLC22A12 gene), an anion exchanger at the apical membrane of the proximal tubule (Enomoto, Kimura et al. 2002). Inhibition of URAT1 is the mode of action of uricosuric drugs (probenecid, sulfinpyrazone, benzbromarone and losartan) (Choi, Mount et al. 2005) discussed later in section 1.8. Other renal urate transporters include Organic Anion Transporter (OAT) 1 and 3 (Cha, Sekine et al. 2001) and multidrug resistance protein 4 (MRP4) (Merriman, Dalbeth 2011). OAT 1 and 3 are basolateral urate transporters and MRP4 is an apical urate export transporter, all of which are likely to be involved in transcellular urate secretion (Hediger, Johnson et al. 2005). A twin study has shown the heritability of renal clearance and excretion of urate to be 60% and 87% respectively, thereby highlighting the genetic predisposition for hyperuricaemia (Emmerson, Nagel et al. 1992).

Rare genetic inborn errors of metabolism may cause endogenous purine production (Merriman, Dalbeth 2011). Deficiency of hypoxanthine guanine phosphoribosyl transferase (Lesch Nyhan syndrome), mutation in the X chromosome gene phosphoribosylpyrophosphate synthetase,

aldolase B and uromodulin genes are all well implicated in the genetic causes of gout (Merriman, Dalbeth 2011). The Genome Wide Association Scanning (GWAS) has also identified an association of gout with de novo mutations in the Methylene Tetrahydrofolate Reductase (MTHFR) (Merriman, Dalbeth 2011), β -3 adrenergic receptor in the Chinese population and the glucokinase regulatory protein (GCKR) genes (Dalbeth, Merriman 2009).

However hyperuricaemia may not necessarily equate to the clinical manifestation of gout, with only 10% of those with hyperuricaemia developing clinical gout (Vitart, Rudan et al. 2008).

1.4 Clinical manifestations of gout

Gout has a predilection for the first metatarsophalangeal joint (MTPJ) (56% - 78% of first attacks) (Roddy, Doherty 2010). Although classically manifesting itself as podagra, gout can affect other joints including the midfoot, ankle, knee and small joints of the hand and wrist (Roddy 2011).

Acute attacks of gout tend to be of sudden onset and self-limiting, reaching peak intensity of pain, swelling and erythema within 24 hours and having complete resolution within 2 to 3 weeks (Zhang, Doherty et al. 2006b). Time between acute attacks of gout is known as the 'inter-critical period' (Roddy, Mallen et al. 2013). When left untreated, MSU crystals continue to accumulate into tophi (hard impacted MSU crystals). Tophi are most likely to be found on toes, fingers, olecranon process, Achilles tendons and helix of the ears (Roddy, Mallen et al. 2013). This chronic tophaceous form of gout can lead to irreversible joint damage, chronic pain and disability (Roddy, Mallen et al. 2013).

1.5 Risk factors for gout

1.5.1 Hyperuricaemia

Hyperuricaemia is the commonest known risk factor for developing gout – a Taiwanese twin study showed an odds ratio of 3.65 (95% confidence interval, CI, 2.72, 5.09) for the prevalence of gout in men with and without SUA > 7 mg/dL (Lin, Lin et al. 2000a). Genetic risk factors for hyperuricaemia have been discussed previously in section 1.3.2. Other population based epidemiological studies have shown an exponential increase in the incidence of gout with increasing levels of SUA (Campion, Glynn et al. 1987; Bhole, De Vera et al. 2010). Conditions associated with under-excretion (chronic kidney disease, use of drugs, metabolic syndrome and genetic factors) or over-production (diet and increased cell turnover in proliferative and inflammatory disorders) of uric acid may be risk factors for hyperuricaemia (Roddy, Mallen et al. 2013; Choi, Mount et al. 2005).

1.5.2 Chronic kidney disease

As the majority of the uric acid is excreted via the kidneys (70%) (Edwards 2008; Lipkowitz 2012), under-excretion due to chronic kidney disease (CKD) may be a risk factor for hyperuricaemia. Hyperuricaemia may occur as a result of reduced glomerular filtration rate and albuminuria (Chen, Wang et al. 2009). Some studies have shown an increased risk of gout in those with pre-existing renal disease, with relative risk (95% CI) ranging from 1.61 (1.60, 1.61) in the Multiple Risk Factor Intervention Trial (MRFIT) (Krishnan 2013) to 4.95 (4.28, 5.72) in the General Practice Research Database (GPRD) study (Mikuls, Farrar et al. 2005a). A Japanese study estimated the incidence of end stage renal disease per 1000 men to be 1.22 in those without hyperuricaemia (SUA >7 mg/dL) compared to 4.64 in men with hyperuricaemia (SUA > 7 mg/dL) (Iseki, Ikemiya et al. 2004). In women the corresponding numbers were 0.87 and 9.03 (hyperuricaemia defined as

>6 mg/dL). Urate-lowering treatment has been demonstrated to improve renal function (Siu, Leung et al. 2006).

1.5.3 Use of diuretics and other drugs

In addition to CKD, patients with gout often have co-morbidities such as hypertension and cardiac disease which require treatment with diuretics. A recent systematic review concluded that the risk of gout was increased in those who were taking diuretics (loop and thiazide) as compared to those not taking diuretics (Hueskes, Roovers et al. 2012). Diuretics may cause hyperuricaemia by inhibiting the renal excretion of uric acid at the organic anion transporter 4 (OAT4) (Hagos, Stein et al. 2007). The increased risk of developing gout in the presence of diuretics reported in several studies are summarised in Table 1-2.

Other anti-hypertensive medications have also been associated with an increased risk of incident gout in a case-control study nested within the GPRD (Choi, Soriano et al. 2012). The relative risk (95% CI) of incident gout with β blockers was 1.48 (1.40 to 1.57), angiotensin converting enzyme inhibitors 1.24 (1.17 to 1.32) and non-losartan angiotensin II receptor blockers 1.29 (1.16 to 1.43) (Choi, Soriano et al. 2012). Conversely, a uricosuric effect was seen with the use of calcium channel blockers (RR 0.87, 95% CI 0.82 to 0.93) and losartan (RR 0.81, 95% CI 0.70 to 0.94) (Choi, Soriano et al. 2012).

Table 1-2: Risk of incident gout with diuretic use

Study	Design	Comparison	RR (95% CI) of gout
Bhole, De Vera et al. 2010	Framingham Heart Cohort Study	Diuretic vs. placebo	Men - 3.41 (2.38, 4.89), women - 2.39 (1.53, 3.74)
Mikuls, Farrar et al. 2005a	GPRD cohort study	Diuretics vs. placebo	1.72 (1.67, 1.76)
Choi, Athinson et al. 2005	Cohort	Diuretic vs. placebo	1.77 (1.42, 2.20)
Grodzicki, Palmer et al. 1997	Cohort	Diuretic vs. placebo	1.59 (0.78, 3.20)
Gurwitz, Kalish et al. 1997	Cohort	Thiazide vs. placebo	1.99 (1.21, 3.26)
Lin, Lin et al. 2000b	Cohort	Diuretic vs. placebo	6.47 (2.03, 8.80)
Hanly, Skedgel et al. 2009	Matched case control	Diuretic vs. placebo	2.80 (2.60, 3.00)
Hunter, York et al. 2006	Case crossover	Loop and thiazide vs. placebo	3.60 (1.40, 9.70)
Abbreviations: GPRD; General Practice Research Database			

1.5.4 Metabolic syndrome

Metabolic syndrome is characterised by hypertension, elevated serum glucose, obesity and hyperlipidaemia (Yamaoka-Tojo, Tojo et al. 2010). In people with gout, the Third National Health and Nutrition Examination Survey (NHANES) found the age and gender adjusted OR of metabolic syndrome to be 3.05 (95% CI 2.01–4.61) compared to people without gout (Choi, Ford et al. 2007). A higher risk of developing gout was seen in obese ($\text{BMI} \geq 30 \text{ kg/m}^2$) men and women in the Framingham Heart Study (RR 2.90, 95% CI 1.89 – 4.44 for men and 2.74, 95% CI 1.65 – 4.58 for women) compared to those with a $\text{BMI} < 30 \text{ kg/m}^2$ (Bhole, De Vera et al. 2010). Similarly a graded association was seen between BMI and risk of incident gout in the Health Professionals Follow-up study (HPFS) of males – the multivariate RR (95% CI) for BMI 23 to 24.9; 1.31 (0.94, 1.83), 25 to 29.9; 1.95 (1.44, 1.65), 30 to 34.9; 2.33 (1.62, 3.36), ≥ 35 ; 2.97 (1.73, 5.10) (Choi, Athinson et al. 2005). Adiposity and insulin resistance are commonly associated with hyperuricaemia (Choi, Mount et al. 2005). The RR of incident type 2 diabetes in men with gout was 1.34 (95% CI 1.09, 1.64) in the prospective Multiple risk Factor Intervention Trial (MRFIT) compared to men without gout (Choi, De Vera et al. 2008). A case control study nested within the GPRD however suggests that diabetes (type 1 more so than type 2 and stronger effect in men than women) has a protective effect on the development of gout through the uricosuric effects of glycosuria (Rodríguez, Soriano et al. 2010) and the impaired inflammatory state seen in diabetes (Choi, Mount et al. 2005). The incidence for gout in those with diabetes compared to those without diabetes was 0.67 (95% CI 0.63 to 0.71) (Rodríguez, Soriano et al. 2010). The risk of incident gout in the presence of distinct components of metabolic syndrome is presented in Table 1-3.

Table 1-3: Incident risk of gout in components of the metabolic syndrome

Study	Design	RR (95% CI)
Obesity		
NHANES (Choi, Ford et al. 2007)	Multistage stratified sampling cohort	2.55 (1.50–4.34),
THIN database (Cea Soriano, Rothenbacher et al. 2011)	Case control	2.34 (2.22 to 2.47)
ARIC study (Maynard, McAdams DeMarco et al. 2012)	Prospective cohort study of females	2.8 (1.33-6.09)
Hyperlipidaemia		
NHANES (Choi, Ford et al. 2007)	Multistage stratified sampling cohort	1.90 (1.24–2.92)
THIN database (Cea Soriano, Rothenbacher et al. 2011)	Case control	1.45 (1.18 to 1.79)
Hypertension		
NHANES (Choi, Ford et al. 2007)	Multistage stratified sampling cohort	2.63 (1.67–4.13),
HPFS (Choi, Athinson et al. 2005)	Prospective cohort study	2.31 (1.96-2.72)
GPRD (Mikuls, Farrar et al. 2005a).	Case control	1.52 (1.48, 1.56)
Framingham Heart Study (Bhole, De Vera et al. 2010).	Prospective cohort	1.59 (1.12 – 2.24) in men and 1.82 (1.06 – 3.14) in women
GPRD (Mikuls, Farrar et al. 2005a)	Case control	1.52 (1.48, 1.56)
Elevated serum glucose		
NHANES (Choi, Ford et al. 2007)	Multistage stratified sampling cohort	1.24 (0.81–1.88)
GPRD (Mikuls, Farrar et al. 2005a)	Case control	1.11 (1.06, 1.16)

Abbreviations: NHANES; National Health And Nutrition Examination Survey, THIN; The Health Improvement Network, ARIC; Arthrosclerosis Risk in Communities study, HPFS; Health Professionals Follow-up Study, GPRD; General Practice Research Database.

1.5.5 Diet and alcohol

The association of diet and alcohol with gout has been examined in several studies nested within the Health Professionals Follow-up Study (HPFS), a longitudinal cohort study of 51,529 male healthcare workers (Choi, Atkinson et al. 2004a; Choi, Atkinson et al. 2004b; Choi, Curhan 2008; Choi, Willett et al. 2007). There was a graded association between the risk of incident gout and intake of sugar sweetened soft drinks (Choi, Curhan 2008). Compared to the intake of less than one sugar sweetened soft drink per month (referent), the multivariate RR (95% CI) for 5 to 6 servings per week was 1.29 (1.00 to 1.68), one serving a day; 1.45 (1.02 to 2.08) and ≥ 2 servings a day; 1.85 (1.08 to 3.16) (Choi, Curhan 2008). The multivariate RR for incident gout also increased with increasing fifths intake of fructose (Choi, Curhan 2008). An increase in multivariate RR (95% CI) of incident gout was also seen with increasing alcohol consumption: 1.32 (0.99–1.75) for 10 to 14.9 g/day, 1.49 (1.14–1.94) for 15 to 29.9 g/day, 1.96 (1.48–2.60) for 30 to 49.9 g/day and 2.53 (1.73–3.70) for ≥ 50 g/day (Choi, Atkinson et al. 2004a). Whereas beer and spirit consumption were both associated with an increased risk of incident gout (RR 1.49 and 1.15 respectively), wine was not (Choi, Atkinson et al. 2004a). A more recent internet based case cross over study however demonstrated an increased risk of recurrent gout attacks (in those who already have gout) with alcohol intake 24 hours prior to the attack, regardless of whether it was wine, beer or liquor consumed (Neogi, Chen et al. 2014).

Men who consumed the highest quintile of total meat intake had a higher multivariate RR (95% CI) 1.41 (1.07 to 1.86) of incident gout compared to men with lowest quintile of meat intake (Choi, Atkinson et al. 2004b). Highest quintile of seafood intake was also associated with higher multivariate RR (95% CI) 1.51 (1.17 to 1.95) of incident gout compared to lowest quintile (Choi, Atkinson et al. 2004b). Consumption of dairy products and coffee had a protective effect on developing gout (Choi, Curhan 2008; Choi, Willett et al. 2007). The contribution of diet and

alcohol in hyperuricaemia may be multi-factorial. Meat and seafood are rich in purines, which are precursors of uric acid. Alcohol and fructose intake facilitate the degradation of adenosine triphosphate (ATP) to adenosine monophosphate (AMP) which can be degraded to uric acid (Woolliscroft, Fox 1986). Alcohol can also reduce uric acid excretion through lactic acidosis (Lieber, Jones et al. 1962). Poor compliance to urate-lowering drugs has also been noted in those with excess alcohol intake (Ralston, Capell et al. 1988). The association of gout with diet and alcohol is summarised in Table 1-4.

Table 1-4: The association of diet and alcohol with the risk of incident gout

Food/alcohol	Design	RR (95% CI)
Meat (Choi, Atkinson et al. 2004).	The HPFS cohort	1.41 (95% CI 1.07 to 1.86) (highest versus lowest quintile)
Low fat dairy products (Choi, Atkinson et al. 2004)		0.56 (95% CI 0.42 to 0.74) (highest versus lowest quintile)
Seafood (Choi, Atkinson et al. 2004).		1.51 (95% CI 1.17 to 1.95) (highest versus lowest quintile)
Sugar sweetened (fructose) soft drinks (Choi HK, Willett W, Curhan G. 2010)	The Nurses Health prospective cohort study (22 year follow-up)	1.62 (95% CI, 1.20-2.19) highest quintile versus lowest quintile
Caffeine (Choi, Curhan 2010)		0.52 (95% CI: 0.41, 0.68 (highest quintile versus lowest quintile)
Alcohol (Cea Soriano, Rothenbacher et al. 2011)	Nested case control in the THIN database cohort study	1 to 9 units/week: 1.06 (1.01 to 1.11)
		>42 units/week: 3.00 (2.66 to 3.38)
Alcohol (Bhole, de Vera et al. 2010)	Nested within the Framingham Heart cohort Study	Women, heavy intake: 3.10 (1.69–5.68) Men heavy intake: 2.21 (1.56–3.14)
Alcohol by category (Neogi, Chen et al. 2014)	Internet based case cross-over study in Boston University	All measures of intake over 24 hours prior to gout attack (referent group 0 servings) Wine >1-2 servings: 2.38 (1.57-3.62) Beer >2-4 servings: 1.75 (1.19-2.59)

Food/alcohol	Design	RR (95% CI)
		>4-6 servings: 2.60 (1.40-4.81)
		Liquor >2-4 servings: 1.67 (1.00-2.78)
		>6 servings: 2.79 (1.26-6.16)

Abbreviations: HPFS; Health Professional Follow-up study, THIN; The Health Improvement Network

1.5.6 Osteoarthritis

Several studies have shown that joints affected by osteoarthritis (OA) are preferred sites for acute attacks of gout and the deposition of tophi (Fam, Stein et al. 1996; Roddy, Zhang et al. 2007a). A cross-sectional study found a strong association between sites affected by acute gout and OA (OR 7.94, 95% CI 6.27,10.05) (Roddy, Zhang et al. 2007a). However due to the cross sectional design of the studies and lack of differentiation between the nature of damage (gout induced or secondary to OA), the temporal relationship between the two remains unclear (Roddy, Doherty 2012). It is clear however that the 1st MTPJ is a frequent target for both gout and OA, although the peak plantar pressures under the 1st MTPJ are higher in OA than gout (Zammit, Menz et al. 2008). This may be due to altered gait pattern which allows quick off-loading of the 1st MTPJ to reduce pain (Rome, Survepalli et al. 2011). Increased permeability of the synovium of the 1st MTPJ to water, thereby allowing its rapid elimination from the joint at night, underpins the increase in concentration of intra-articular urate crystals and sudden onset of podagra at night (Simkin 1977).

1.6 Gout and cardiovascular diseases

In addition to metabolic syndrome, osteoarthritis, chronic kidney disease, gout is associated with ischaemic heart disease and congestive heart failure (Mikuls, Farrar et al. 2005a; Zhu, Pandya et al. 2012). The relationship between gout and cardiovascular diseases may be multi-factorial (due to immobility, non-steroidal anti-inflammatory drugs, chronic systemic inflammation causing a proatherogenic state) (McGettigan, Henry 2011; Brook, Yalavarthi et al. 2011). However the increased vascular risk in gout may also be confounded by the presence of shared risk factors such as hypertension and obesity (Choi 2005). A recent systematic review and meta-analysis reported increased cardiovascular disease (CVD) (pooled HR 1.29, 95% CI 1.14–1.44) and coronary heart disease (CHD) mortality (pooled HR 1.42, 95% CI 1.22–1.63) in gout despite adjustments for traditional vascular risk factors (Clarson, Chandratre et al. 2013). The persistent state of inflammation (Soltész, Kerekes et al. 2011) and hyperuricaemia (Kim, Guevara et al. 2010) have both been suggested as gout-specific risk factors for CVD and CHD mortality. No association was seen however between gout and mortality from myocardial infarction (MI) (Clarson, Chandratre et al. 2013), a finding supported elsewhere. The 17 year follow up of 9105 men in the Multiple Risk Factors Intervention Trial (MRFIT) (Krishnan, Svendsen et al. 2008) concluded that there was a non-significant rise in mortality from MI in males with gout. The non-significant relationship between mortality from MI and gout may be attributed to misclassification of MI as CVD or CVD and surveillance bias leading to prevention of CHD from progressing into MI (Clarson, Chandratre et al. 2013). Never the less an increased multivariate OR (95% CI) of 1.26 (1.14, 1.40) of acute MI in those with gout compared to those without gout has been reported in a case-control study nested within the MRFIT study (Krishnan, Baker et al. 2006). A 7 year cohort study nested within the British Columbia Linked Health Database (BCLHD) (De Vera, Rahman et al. 2010) concluded that the multivariate adjusted RR (95% CI) for all MI amongst women with gout compared to women without gout was 1.39 (1.20, 1.61).

A recent Taiwanese cohort study of those with hyperuricaemia but not gout has also shown a U shaped relationship between levels of uric acid and mortality from CVD (Kuo, See et al. 2013). Even after adjusting for age, gender and traditional risk factors, a HR (95% CI) of 1.21 (1.14, 1.29), 1.74 (1.60, 1.88) and 2.53 (2.28, 2.81) was seen for cardiovascular mortality for corresponding uric acid strata 0.42–0.53, 0.54–0.65 and ≥ 0.66 mmol/l compared to 0.30 to 0.41 as referent group (Kuo, See et al. 2013).

1.7 The treatment of acute gout

1.7.1 Colchicine

The earliest reported use of colchine was by the Byzantine physician Alexander of Tralles (Copeman 1964). An alkaloid derived from the autumn crocus (*Colchicum autumnale*), colchicine acts by inhibiting neutrophil influx and migration through its interaction with E selectins on endothelial cells (Cronstein, Terkeltaub 2006). A randomised placebo controlled trial concluded that low dose colchicine (cumulative dose of 1.8 mg in 24 hours) had equal efficacy and better side effect profile (diarrhoea and vomiting) compared to higher dose of 4.8 mg over 24 hours (Terkeltaub, Furst et al. 2010). However due to its side-effects and interaction with other medications (statins, amiodarone, verapamil, macrolide antibiotics to name a few (Roddy, Mallen et al. 2013)), colchicine is often superseded by Non-Steroidal Anti Inflammatory Drugs (NSAIDs) as first line, followed by cyclooxygenase 2 (COX 2) inhibitors and glucocorticoids.

1.7.2 Non-Steroidal Anti Inflammatory Drugs

At present there is no evidence to suggest the superiority of one NSAID over another or over COX2 inhibitors (Sivera, Andrés et al. 2013). Although indomethacin (50 mg three times a day) has been shown to be as effective as etoricoxib (120 mg a day) and oral prednisolone, its use is

not recommended due to high risk of gastrointestinal toxicity (Sutaria, Katbamna et al. 2006; Rubin, Burton et al. 2004; Man, Cheung et al. 2007). The use of NSAIDs is best avoided in the presence of cardiovascular and renal disease, which coexist in a large proportion of patients with gout.

1.7.3 Other treatments

In the presence of cardiovascular and renal co-morbidity and when multiple joints are involved in an acute attack of gout, corticosteroids (oral or intramuscular) are often the treatment of choice (Khanna, Fitzgerald et al. 2012). Oral prednisolone 30 to 35 mg for five days is as effective as NSAIDs (Man, Cheung et al. 2007; Janssens, Janssen et al. 2008). Based on evidence from an uncontrolled trial (Fernandez, Noguera et al. 1999), a fast and effective relief of pain and intra-articular hypertension (in addition to aiding diagnosis through aspiration of synovial fluid and identification of MSU crystals) may be provided by intra articular injection of corticosteroid, particularly when the inflammation is mono or oligoarticular (Khanna, Fitzgerald et al. 2012). Although limited by expense and lack of license to be used in gout in the UK, when above treatments are contra-indicated or impractical, biologic drugs may be considered (Rees, Hui et al. 2014). Rilonacept (soluble receptor fragment fusion protein which inhibits IL 1 α and β), canakinumab (humanised IL 1 β monoclonal antibody) and anakinra (recombinant non-glycosylated IL 1R α) are yet to be approved for the treatment of gout in the UK (Burns, Wortmann 2011).

1.8 Treatment of chronic gout

Whereas there are no guidelines to suggest the prioritisation of one treatment over the other in the treatment of acute gout, allopurinol is clearly the first line drug to treat recurrent attacks (chronic) gout (Sivera, Andrés et al. 2013). Although it started off as an anti-neoplastic medication

(Elion 1989), its uric acid-reducing properties led to its approval for the treatment of gout in 1966 by the US food and Drug Administration (FDA) (Terkeltaub 2003). Allopurinol is an analogue of the purine bases hypoxanthine and xanthine, and binds competitively to xanthine oxidase thereby preventing the conversion of xanthine to uric acid (Murrell, Rapeport 1986). The dose of allopurinol can be titrated (usually in 100 mg increments, with a maximum dose of 900 mg per day) to reduce the concentration of SUA below the saturation threshold (6 mg/dL) which facilitates the dissolution of pre-existing tophi and prevents progression to irreversible cartilage and bone damage (Terkeltaub 2003).

Those who are intolerant to allopurinol (side-effects are rare but can be severe and include allopurinol hypersensitivity syndrome in those with renal impairment) may benefit from febuxostat, a non-purine based xanthine oxidase inhibitor, which had a greater reduction in SUA compared to fixed dose allopurinol (300 mg) (Becker, Schumacher et al. 2005) or uricosuric drugs (Sivera, Andrés et al. 2013). The use of high dose (4 – 6 grams/day) aspirin in the 19th century to promote renal excretion of uric acid (Gutman 1959) is no longer advocated, due to potential side effects such as increased risk of bleeding. Other uricosurics such as sulfinpyrazone and probenecid may be less effective at reducing SUA compared to allopurinol (Scott 1966) but are a viable alternative in those who are intolerant to or have disease refractory to allopurinol (Zhang, Doherty et al. 2006a). Benzbromarone is more effective at reducing SUA compared to allopurinol but its use is restricted due to the potential side effect of hepatotoxicity (Perez-Ruiz, Calabozo et al. 1999). Pegylated uricase (Becker, Baraf et al. 2012) converts urate to allantoin which is more readily excreted (Burns, Wortmann 2011) and has been licensed in Europe for use in 'treatment refractory gout' (Rees, Hui et al. 2014). Although effective in reducing uric acid (Sundy, Baraf et al. 2011), there are on-going concerns about adverse reactions due to its antigenic properties, risk of cardiovascular disease and development of antibodies towards the PEG component of the drug

with repeated infusions (Ganson, Kelly et al. 2006). Other medications with modest uricosuric effects are losartan, vitamin c and fenofibrate, all of which are used as adjunctive treatments in gout as they are unlikely to achieve therapeutic target level of uric acid on their own (Stamp, O'Donnell et al. 2013).

Although the initiation of ULT is recommended in those with recurrent attacks of gout, tophi, radiographic evidence of joint damage, renal insufficiency and uric acid urolithiasis (Jordan, Cameron et al. 2007) (Zhang, Doherty et al. 2006a), clinical practice remains widely variable. ULT may be started after the first attack of gout when the crystal load in and around joints is still low (Zhang, Doherty et al. 2006a), or it may be postponed until two or more attacks per year (Khanna, Fitzgerald et al. 2012). ULT is usually initiated once the acute attack subsides (usually 2 to 4 weeks) to reduce the risk of drug induced acute gout (Roddy, Mallen et al. 2013). Treatment with ULT is usually life long, SUA should be monitored yearly and maintained below 6 mg/dL (saturation threshold) once a stable dose of ULT has been reached (to correspond with no further attacks of gout) (Zhang, Doherty et al. 2006a).

Despite clear guidelines and multitude of treatment options, gout remains poorly treated due to physician and patient related factors (Doherty, Jansen et al. 2012). Although health care professionals feel that they have adequate knowledge to manage gout (Harrold, Mazor et al. 2010), they often focus solely on treating the acute attack and fail to recognise the long-term consequences of chronic gout (irreversible joint damage due to on-going MSU crystal deposition, impaired health related quality of life and higher risk of developing associated conditions such as hypertension, renal impairment and cardiovascular diseases) (Singh, Strand 2008; Lindsay, Gow et al. 2011). Once initiated, allopurinol is not always titrated to achieve the desired SUA < 6 mg/dL (Doherty, Jansen et al. 2012) with some evidence that the lower the SUA, the faster the

dissolution of crystals and therefore cure (Perez-Ruiz, Calabozo et al. 2002a). Patients are often not made aware of the rationale behind lifelong ULT and the possibility of drug induced attack of gout in the absence of prophylactic treatment with NSAIDs or colchicine (which they mistakenly consider treatment failure or side effect) (Weaver, Cheh et al. 2008). Colchicine is more effective than placebo in reducing the number and severity of attacks during the first 3 to 6 months of initiation of ULT to treat recurrent attacks of gout (Borstad, Bryant et al. 2004). Information on rationale behind ULT may improve adherence to treatment (Ogdie, Hoch et al. 2010).

1.9 Health Related Quality of Life

1.9.1 Concepts and definitions

Health has been defined as “a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity”². Quality of life (QOL) is a multidimensional concept (Taillefer, Dupuis et al. 2003) which includes negative and positive aspects of life ranging from death to happiness (Guyatt, Feeny et al. 1993) and is influenced by personal beliefs, values, culture and the environment (Wilson, Cleary 1995).

QOL is often used interchangeably with other terms such as ‘functional disability’, ‘subjective wellbeing’, ‘life satisfaction’ and ‘health status’ (Revicki, Rentz et al. 2011). Clinicians are mostly concerned with Health Related Quality of Life (HRQOL) to focus on aspects directly concerned with health and exclude the less clinically relevant ones. However in reality, all aspects of life influence health in one way or other (Guyatt, Feeny et al. 1993) Therefore HRQOL can be seen as an umbrella term that encompasses at least seven domains of life: material well-being, health, productivity, intimacy, safety, community and emotional well-being (Taillefer, Dupuis et al. 2003).

² The International Health Conference, New York, 19-22 June, 1946.

Although multiple definitions of HRQOL have been produced (Table 1-5), all seem to share key features incorporating the influence of multiple aspects of life on well-being and functional status as assessed by the patients themselves.

Table 1-5: Definitions of HRQOL

Source	Definition
Patrick and Erikson. 1993, p.419	<i>“The value assigned to the duration of life as modified by impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy”.</i>
The WHO group (Skevington, Lotfy et al. 2004, p.299)	<i>“Individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the persons' physical health, psychological state, level of independence, social relationships and their relationship to salient features of their environment”</i>
Bowling, and Press. 2001, p.2	<i>“It is multi-dimensional and theoretically incorporates all aspects of an individual's life – optimum levels of mental, physical, role (e.g. work, parent, carer, etc.) and social functioning, including relationships and perceptions of health, fitness, life satisfaction and well-being”.</i>
Testa, Simonson 1996, p.835	<i>“Physical, psychological and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations and perceptions”</i>

1.9.2 Why consider HRQOL?

HRQOL can be considered a universal indicator of health status, service needs and effects of intervention thereby facilitating clinical decision-making and policy implementation (Kindig, Stoddart 2003). The UK Department of Health has identified HRQOL and health status as key components of patient outcome assessments alongside the more traditional markers such as survival rates (Hickey, Barker et al. 2005). Traditional measures of disease and treatment outcomes (in gout for example, laboratory investigations – serum uric acid level and clinical examination findings –tophi) are over-simplistic and may not take into account the factors that may impair HRQOL and ultimately lead to non-adherence to treatment. Whereas traditional objective measures are of greater interest to healthcare providers, they may not reflect the functional and psychosocial well being of an individual, which are key areas of interest for patients and are captured by HRQOL assessments (Guyatt, Feeny et al. 1993). Measuring HRQOL in chronic diseases also identifies risk factors associated with, or predictive of, adverse outcomes. Individuals or population groups at risk of poor outcome may then be targeted with interventions which may improve their health and functional status. Surveillance of HRQOL is also important in an ageing population with increasing life expectancy so that the quality of the additional years lived are reflective of the advances in healthcare despite the changes associated with a normal ageing process (John, Kirby et al. 2003). HRQOL measurements can be used in the following domains (Fitzpatrick, Fletcher et al. 1992):

- Screening and monitoring for psychosocial problems in individual patient care
- Population surveys of perceived health problems
- Medical audit
- Outcome measures in health services or evaluation research
- Clinical trials
- Cost-utility analyses

1.9.3 HRQOL in gout in the context of other chronic diseases

Gout is a complex and excruciatingly painful inflammatory arthritis associated with significant risk factors such as obesity, hypertension, diabetes, ischaemic heart disease, chronic kidney disease and treatment with diuretics (Doherty, Jansen et al. 2012; Choi, Ford et al. 2007). Previously the prevalence of gout has been associated with increasing deprivation and non-Caucasian ethnicity (Taylor, Smeets et al. 2004). A recent study of gout and socio-economic status using questionnaire and electronic medical record linkage showed an association of lack of further education (univariate analysis only) and inadequate income with gout (Hayward, Rathod et al. 2013). Being a multi-dimensional concept HRQOL in a chronic disease such as diabetes is affected by long treatment periods, frequent healthcare consultations, pain, fatigue, sleep disturbance, depression and disability (Ragnarson Tennvall, Apelqvist 2000; Schlenk, Erlen et al. 1997; Baumstark, Buckelew 1992). HRQOL in asthma was associated with socio-demographic characteristics in addition to disease severity (Apter, Reisine et al. 1999). Although weak, there was some evidence to support that asthma control (night time awakenings) was poor in ethnic minority groups, those with poor household income, low education level and unemployed (Apter, Reisine et al. 1999). Socio-economic status was in fact associated with poor HRQOL independent of severity of asthma (Apter, Reisine et al. 1999).

Given the complex links between gout, co-morbidities and socio-demographic characteristics, HRQOL in gout is likely to be associated with all these patient characteristics (Roddy, Zhang et al. 2007c; Brunner, KleinGitelman et al. 2004). This is supported by the fact that the conceptual model of HRQOL includes biological and physiological variables, symptoms, functional status, general health perceptions and is underpinned by individual, environmental and non-medical characteristics (Wilson, Cleary 1995). Most of the existing studies have not included a comprehensive assessment of socio-demographic and co-morbid characteristics in assessing

HRQOL in gout. For example, increasing frequency of attacks and tophi were associated with poorer HRQOL after adjusting for age and gender in a European and US based cross-sectional study (Khanna, Nuki et al. 2012) and a cohort study of treatment failure gout (Becker, Schumacher et al. 2009). These studies however had not adjusted for co-morbid conditions associated with gout. Only one UK based primary care study has shown that the presence of musculoskeletal and medical co-morbidity in gout is also associated with poor HRQOL (Roddy, Zhang et al. 2007c). Evidence for the association of HRQOL with traditional objective measure such as SUA (commonly used as an outcome measure in clinical trials as well as clinical practice) remains weak (De Klerk, Van Der Heijde et al. 2003; Becker, Schumacher et al. 2009). This further strengthens the case for patient-reported HRQOL as an outcome measure in gout (De Klerk, Van Der Heijde et al. 2003). The Outcome Measures in Rheumatology clinical Trials 9 (OMERACT 9) group have in fact endorsed HRQOL as a core domain to be included in the assessment of outcomes in clinical trials of chronic gout (Schumacher, Taylor et al. 2009).

1.9.4 How should HRQOL in gout be measured?

In the OMERACT 9 meeting, the principal outcomes of concern to patients with gout were: pain, loss of mobility, fear of medication side-effects, loss of sleep, emotional stress, work and social limitation, joint deformity and dependency on others (Schumacher, Taylor et al. 2009). In order to capture all of these constructs, generic (Health Assessment Questionnaire Disability Index (HAQ-DI) and Short Form 36 (SF-36)) and disease-specific (Gout Impact Scale (GIS) developed from the revised Gout Assessment Questionnaire 2.0 (GAQ 2.0)) questionnaires have been used in existing studies of chronic gout. The HAQ-DI forms part of the Health Assessment Questionnaire (HAQ), developed in 1980 to measure health status in chronic diseases (Bruce, Fries 2003b). The HAQ-DI specifically measures functional ability through questions focused on fine movements of the upper limbs and locomotor activities of the lower limbs. The HAQ-DI also includes a Visual

Analogue Scale (VAS) to assess arthritis related pain and its severity over the course of the past one week (Bruce, Fries 2003b). The SF-36 measures functional limitation through its Physical Function-10 (PF-10) subscale (White, Wilson et al. 2011). The PF-10 specifically asks subjects whether health limits their physical activity, mobility and activities of daily living through questions pertaining to a variety of physical activities ranging from easy to strenuous (White, Wilson et al. 2011). The advantage of generic instruments (health profiles and utility measures) lies in their ability to measure all important aspects of HRQOL and use in any population. They also enable comparison across different conditions and interventions and cost- utility analysis (Guyatt, Feeny et al. 1993). Generic instruments, nevertheless, may be less responsive to change in specific conditions (Mazur, Kupiainen et al. 2011). Disease-specific instruments are more focused on the characteristics of the condition in question and are more likely to be responsive to clinical changes in the condition. Patients may feel that the questionnaire is directly relevant to their specific condition. However, such specific questionnaires do not allow comparison between disease states (Guyatt, Feeny et al. 1993). Unlike other rheumatic conditions, there had been a paucity of validated gout-specific questionnaires to measure HRQOL until the advent of the GIS in 2008 (Hirsch, Lee et al. 2008). However relatively new and yet to be endorsed by OMERACT (Grainger, Taylor et al. 2009), the GIS needs to be evaluated in further longitudinal studies. At present, only the HAQ-DI and SF-36 has been approved as a validated tool to measure HRQOL (Grainger, Taylor et al. 2009) in gout by the OMERACT 9 group. In order to be endorsed by OMERACT, the instruments need to demonstrate robust measurement properties.

1.10 Measurement properties of instruments used to measure HRQOL

The instrument used to measure HRQOL should show transparency and robustness of the following measurement properties (Terwee, Bot et al. 2007):

1.10.1 Face validity

This is the minimum subjective measure of validity. This simply assesses by inspection whether the scale measures what it is intended to measure (Albers, Ecteld et al. 2010). In a study of the development of the Gout Assessment Questionnaire (GAQ 2.0) (Hirsch, Lee et al. 2008), two focus groups of participants with gout approved 14 items assessing the impact of gout on HRQOL, therefore supporting face and content validity, discussed below.

1.10.2 Content validity

This is a measurement of whether the items of a scale measure the relevant aspects of the construct being measured (Guyatt, Feeny et al. 1993). It also includes floor and ceiling effects – extreme scores which fail to differentiate between participants at either end. There are no opportunities to show improvements or deterioration. The HAQ-DI for example has been reported to have high ceiling effect, with 34% participants in a study of functional disability in patients with gout (Ten Klooster, Oude Voshaar et al. 2011) scoring no disability.

1.10.3 Concurrent or criterion validity

This is the correlation between the scale being assessed (new) with an established and validated scale which measures the same construct in the same sample set at the same time. The better the correlation, the more confidence can be placed in the new measure. The previously validated scale serves as a criterion or 'gold standard' (Guyatt, Feeny et al. 1993). For example, the HAQ-II and PF-10 were strongly correlated with the HAQ-DI (Spearman's correlation HAQ II: HAQ-DI 0.87 and PF-10: HAQ-DI -0.75) (Ten Klooster, Oude Voshaar et al. 2011).

1.10.4 Construct validity

In the absence of a gold standard, this refers to the extent to which the observed scores are in keeping with other measures or characteristics that are associated with the construct being measured. It confirms or refutes a pre-specified hypothesis in the context of the theoretical expectations and conceptualisations (Albers, Ecteld et al. 2010). For example, those with lower self and physician-rated gout severity, frequency of attacks and attack pain were hypothesized to have lower scores in the Gout Impact (GI) section of the GAQ 2.0 (lesser impact of gout on HRQOL) (Hirsch, Lee et al. 2008). Known groups and triangulation are variations of construct validity. In the above-mentioned study of functional disability in gout (Ten Klooster, Oude Voshaar et al. 2011), known group validity was better for the HAQ II and HAQ-DI compared to PF-10. Those in the self-reported good health category scored higher in the PF-10 (higher scores represent better health) than those in the excellent health category.

1.10.5 Internal consistency

It measures the correlation between items in a scale or a subscale. Items measuring a certain dimension of the construct should have good internal consistency with other items measuring the same dimension but not with items measuring some other dimension of the construct (Albers, Ecteld et al. 2010). For the GI part of the GAQ 2.0 (Hirsch, Lee et al. 2008), items of all except unmet treatment need and medication side-effects subscales had sufficient consistency with each other, as shown by alpha coefficients approximately or equal to 0.80 (Nunnally 1967).

1.10.6 Test re-test reliability

This measures the correlation between scores from the same participant at two different time points. There needs to be a careful balance between sufficient time interval to avoid recall bias and too great a time lag allowing the characteristic under investigation to change (Albers, Ecteld

et al. 2010). In the study of the development of the GAQ 2.0 (Hirsch, Lee et al. 2008), 21% of the patients at baseline completed the same questionnaire at a 2 week interval and each scale of the questionnaire showed good test retest reliability (Interclass correlation coefficient, ICC > 0.70) (Fitzpatrick, Davey et al. 1998).

1.10.7 Agreement

Measurement error quantifies the lack of agreement between two different measurements. Measurement error can be random or systematic. It is possible to account for systematic error but not for random error. The standard error of measurement (SEM) or the smallest detectable change (SDC) must be smaller than the minimal important change (MIC) (Albers, Ecteld et al. 2010). Not all measurement properties however may equally important – content validity may be the first and most important desired quality of an instrument (Terwee, Bot et al. 2007). The aim of the study may demand different measurement properties in terms of responsiveness and reliability. Discriminative studies may require a high level of reliability to distinguish between participants but may not necessarily be responsive to change. Evaluative studies may require high levels of agreement to detect important change (Terwee, Bot et al. 2007).

1.11 Conclusion

This chapter provided an overview of the pathogenesis, clinical manifestations, epidemiology and treatment of gout. It also highlighted the relevance of HRQOL in the context of gout and the need for further primary care-based research in this domain. The next chapter therefore outlines the aims and objectives of the thesis relating to the study of HRQOL in primary care.

2 Aims, objectives and structure of the thesis

2.1 Introduction

This chapter presents the aims, objectives and methodological overview of the thesis. An overview of the thesis structure and the purpose of each of the chapters included within it are also presented.

2.2 Thesis statement

Gout is the commonest inflammatory arthritis affecting 2.49% of the population in the UK (Kuo, Grainge et al. 2014) and is associated with poor Health Related Quality of Life (HRQOL) through its disease characteristics (Becker, Schumacher et al. 2009) as well as associated co-morbidities (Singh, Strand 2008). HRQOL in gout in primary care in the UK is under-researched (one existing study only (Roddy, Zhang et al. 2007c)) and poorly understood, which may contribute to the sub-optimal management of gout in primary care (Roddy, Zhang et al. 2007b). Other existing international studies have been based in secondary care or specialist settings and used either generic or gout-specific measures of HRQOL but not the two together (Becker, Schumacher et al. 2009) (Singh, Strand 2008).

2.3 Aims and objectives

The aims and objectives of the thesis were as follows:

Aim 1

- 1 To provide a description of HRQOL in gout and examine the methods used to measure HRQOL in existing studies

Objectives

- a) To investigate which questionnaires have previously been used to measure HRQOL in gout
- b) To examine the robustness of the clinimetric properties of the questionnaires previously used
- c) To determine the distribution of the scores of HRQOL in these studies
- d) To determine which factors have previously been found to associate with poor HRQOL in gout

Aim 2

To describe HRQOL scores stratified by gout-specific, co-morbid and socio-demographic characteristics in this study.

Objectives

- a) To compare non-responders and responders to the baseline questionnaire by age, gender and neighbourhood deprivation
- b) To describe the gout, co-morbid and socio-demographic characteristics of responders to the baseline questionnaire
- c) To describe the range of scores of the gout-specific Gout Impact Scale (GIS) and generic Health Assessment Questionnaire Disability Index (HAQ-DI) and Physical Function (PF-10) and their stratification by gout, co-morbid and socio-demographic characteristics (univariate unadjusted analysis)

Aim 3

To identify which gout-specific, co-morbid and socio-demographic characteristics are associated cross-sectionally with HRQOL

Objectives

To test the association of gout-specific, co-morbid and socio-demographic characteristics with HRQOL measured using the GIS, PF-10 and HAQ-DI using linear regression model unadjusted and adjusted for measured confounding factors (gout, co-morbid and socio-demographic).

Aim 4

To explore patient experience of gout focussing on impact of gout and its treatment on HRQOL.

Objectives

To explore the patients' experiences, beliefs and attitudes on which gout and treatment characteristics affect HRQOL and how, using focus group interviews.

2.4 Study design

Primarily conducted as a quantitative enquiry, the thesis adopts a positivist stance (Bowling 2009) – it aims to ascertain objective reality or 'positive facts' which are measurable and undistorted by the 'value judgement' of the researcher (Keat 1979). However positivism does not attempt to understand the meaning of facts within situational context or 'meaning of situations to people' (Bowling 2009). Therefore to provide a richer contextual meaning to the results, a qualitative

approach was embedded within this thesis. A phenomenological approach (Bowling 2009) underpins the qualitative research component of this thesis – it acknowledges that fact or reality may be interpreted by its meaningfulness to participants and is often socially constructed after interaction with each other (Smart 2013).

Although diametrically different, the two approaches (positivism and phenomenology) used together complement the nature of enquiry in this thesis. The two distinct studies within this thesis use quantitative and qualitative methodology to provide measurable associates of HRQOL and a personalised interpretation or confirmation of the ‘accuracy, content, validity and relevance’ (Bowling 2009) of these (and other novel) findings within a population (epidemiological) context. It is hoped that by using mixed methodology, the understanding of which factors affect HRQOL can be extended further to ‘why’ and ‘how’ they do so.

2.5 Methodological overview

All quantitative analyses in this thesis use cross-sectional data obtained from the baseline stage of a primary care-based cohort study (baseline questionnaire in appendix 3). The qualitative study of the impact of gout and its treatments on HRQOL was nested within the cross-sectional study by interviewing selected responders to the questionnaire. The aim-specific methods are as follows:

Aim 1: Systematic literature search and narrative synthesis (published literature)

Aim 2 and 3: Cross-sectional epidemiological analysis (patient-reported and clinical data from medical record review)

Aim 4: Thematic analysis of qualitative data (focus group interview narratives)

2.6 Thesis structure

The thesis is comprised of nine chapters, described in Figure 1. The quantitative analysis of the questionnaire data (chapters 5 to 7) is linked with results of the preceding chapter informing the next. The focus group interviews comprising the qualitative study chapter were conducted concurrently with the questionnaire survey but predated quantitative data analyses. As the interviews were open-ended rather than prescriptive, they were not designed to direct responses towards detailed explanations (why and how) of factors identified to affect HRQOL in the questionnaires. However the findings from the qualitative studies were used to provide contextual depth to the quantitative results (see chapter 8). A brief outline of each chapter is provided below:

Chapter 1: The concept of Health Related Quality of Life in gout

An overview of gout and HRQOL in this context as well as rationale for further research was discussed in the previous chapter.

Chapter 3: Health Related Quality of Life in gout: A systematic search and overview

A narrative synthesis of the existing studies on HRQOL in gout, as well as an assessment of the clinimetric properties of questionnaires used to measure HRQOL in gout. The associations of poor HRQOL (gout as well as co-morbid and socio-demographic characteristics where relevant) in existing studies will also be presented.

Chapter 4: A cross-sectional study of Health Related Quality of Life in gout: design and methods

This chapter provides details of the design and methods used to conduct the cross-sectional survey and nested focus group interviews. Although nested within a larger longitudinal cohort study (see previously published protocol (Chandratne, Mallen et al. 2012)), chapter 4 only describes the methods relevant to the cross-sectional phase of the study.

Chapter 5: Cross-sectional survey of Health Related Quality of Life in gout: Response and responder characteristics

This chapter describes the flow of participants through the cross-sectional study (quantitative) and compares responders to non-responders in terms of socio-demographic characteristics.

Chapter 6: The association of gout, co-morbid and socio-demographic characteristics with Health Related Quality of Life: Univariate analysis

This chapter describes the HRQOL scores distributed by responders' gout, co-morbid and socio-demographic characteristics. It compares the mean HRQOL scores amongst responders grouped by the above characteristics.

Chapter 7: The cross-sectional associations of gout-specific, co-morbid and socio-demographic characteristics with Health Related Quality of Life: A linear regression analysis

This chapter describes which gout-specific, co-morbid and socio-demographic characteristics are independently associated with HRQOL by using linear regression models with crude and adjusted analyses.

Chapter 8: The impact of gout and its treatments on Health Related Quality of Life: A qualitative study of participants' perspectives using focus group interviews

This chapter provides an insight into the participants' experiences, beliefs and attitudes towards how gout and its treatments may affect HRQOL. As the methods have been described in detail in chapter 4, this chapter focuses on the thematic analysis of interview transcripts. In order to keep the themes close to the participants' views, extracts from the interviews are embedded as quotations within the results.

Chapter 9: Thesis conclusions and implications for clinical practice and further research

An overall summary of the main findings of each of the analyses within this thesis are presented within this chapter. A critical evaluation of the interpretation of these findings and their implications for clinical practice are also discussed. Finally, suggestions for future research based upon the findings of this thesis are presented.

2.7 Conclusion

This chapter has presented the aims of the thesis and objectives used to fulfil these aims. The study components and methodology used were also discussed here. Finally an overview of the thesis plan with brief description of each chapter was presented. The next chapter will address aim 1 by systematically reviewing the existing literature on HRQOL in gout.

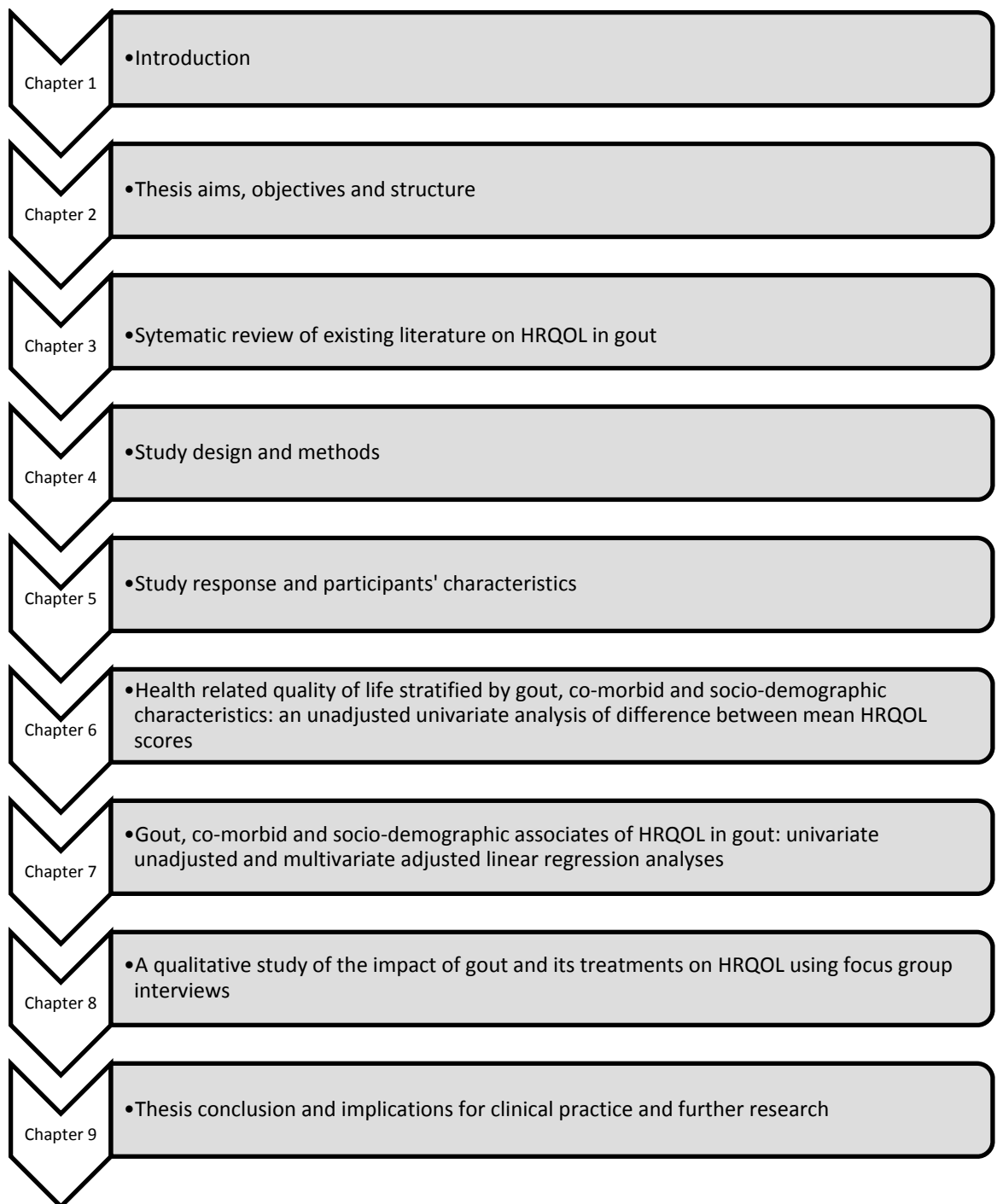


Figure 1: Flow diagram summarising thesis structure

3 Health Related Quality of Life (HRQOL) in gout: A systematic search and overview

3.1 Introduction

The first chapter presented the background to gout and the concept of HRQOL as a multidimensional phenomenon influenced by a multitude of factors including disease, its treatment and cultural perspectives. It then highlighted the ways in which gout could be associated with poor HRQOL. This chapter presents a systematic search and review of the existing literature on HRQOL in gout. It describes the range of questionnaires used to measure HRQOL in gout and assesses their quality against previously defined measurement standards. Finally it presents the gout-specific factors that have been associated with HRQOL in existing studies.

3.2 Aims

The aim of this chapter is to provide an overview of the existing literature on the gout-specific characteristics that are associated with or predictive of HRQOL and examine the methods used to measure HRQOL in gout.

3.3 Objectives

The specific objectives of this systematic review were as follows:

- I. To investigate the range of instruments used to measure HRQOL in gout in existing studies
- II. To examine the robustness of the clinimetric properties of these instruments
- III. To determine the scores of HRQOL in existing studies of gout
- IV. To identify which factors have previously been found to associate with poor HRQOL in gout.

3.4 Methods

3.4.1 Search strategy

A systematic search was undertaken using the following databases from inception to October 2012: MEDLINE, EMBASE, CINAHL, PsycINFO and Cochrane database of systematic reviews. Search for the construct of HRQOL included terms such as 'health status', functional status', 'quality of life', 'health related quality of life' and 'questionnaires'. The population search included the following terms: 'gout' and 'gout suppressants'. In order to identify articles presenting the clinimetric properties of questionnaires used to measure HRQOL in gout, a range of search terms pertaining to measurement properties were adapted from Terwee, Jansma et al. 2009 and are presented in Table 3-1 below. In order to identify all articles on HRQOL in gout (including ones with empirical data on HRQOL as well as those presenting clinimetric properties of questionnaires used to measure HRQOL) the construct and population searches were combined with each other and with the filters for measurement properties. To increase the recall of the search results, all terms were typed as synonyms and 'free text' and mapped to thesaurus. Truncated terms and wildcards were used specific to each database.

Table 3-1: Search terms to identify all articles on HRQOL in gout

Construct search

"QUALITY OF LIFE"/, "OUTCOME ASSESSMENT (HEALTH CARE)"/ OR "OUTCOME AND PROCESS ASSESSMENT (HEALTH CARE)"/ OR TREATMENT OUTCOME/employment/ **(OR)**

Instrument search

HEALTH SURVEYS/ HEALTH STATUS INDICATORS/ DISABILITY EVALUATION/
questionnaire*.ti,ab, QUESTIONNAIRES/ **(OR)**

Population search

GOUT/ OR GOUT SUPPRESSANTS/

Filter for measurement properties

instrumentation.ti,ab, methods.ti,ab, ((validation stud*).pt, ((comparative stud*).ti,ab, PSYCHOMETRICS/, psychometr*.ti,ab, clinimetr*.ti,ab, clinometr*.ti,ab, "observer variation".ti,ab, OBSERVER VARIATION/, "REPRODUCIBILITY OF RESULTS"/, reproducib*.ti,ab, DISCRIMINANT ANALYSIS/, reliab*.ti,ab, unreliab*.ti,, valid*.ti,ab, coefficient.ti,ab, homogeneity.ti,ab, homogeneous.ti,ab, "internal consistency".ti,ab, ((cronbach* AND alpha*).ti,ab, ((item AND (correlation* OR selection* OR reduction*))).ti,ab, agreement.ti,ab, precision.ti,ab, imprecision.ti,ab, "precise values".ti,ab, test-retest.ti,ab, ((test AND retest)).ti,ab, ((reliab* AND (test OR retest))).ti,ab, stability.ti,ab, interrater.ti,ab, inter-rater.ti,ab, intrarater.ti,ab, intra-rater.ti,ab, intertester.ti,ab, inter-tester.ti,ab, intra-tester.ti,ab, intratester.ti,ab, interobserver.ti,ab, inter-observer.ti,ab, intraobserver.ti,ab, intra-observer.ti,ab, intertechnician.ti,ab, inter-technician.ti,ab, intratechnician.ti,ab, intra-technician.ti,ab, interexaminer.ti,ab, inter-examiner.ti,ab, intraexaminer.ti,ab, intra-examiner.ti,ab, interassay.ti,ab, inter-assay.ti,ab, intraassay.ti,ab, intra-assay.ti,ab, interindividual.ti,ab, inter-individual.ti,ab, intraindividual.ti,ab, intra-individual.ti,ab, interparticipant.ti,ab, inter-participant.ti,ab, intraparticipant.ti,ab, intra-participant.ti,ab, kappa.ti,ab, kappa's.ti,ab, kappas.ti,ab, repeatab*.ti,ab, (((replicab* OR repeated) AND (measure OR measures OR findings OR result OR results OR test OR tests))).ti,ab, generaliza*.ti,ab, generalisa*.ti,ab, concordance.ti,ab, ((intraclass AND correlation*).ti,ab, discriminative.ti,ab, "known group".ti,ab, "factor analys*".ti,ab, dimension*.ti,ab, subscale*.ti,ab, ((multitrait AND scaling AND (analysis OR analyses))).ti,ab, (item AND

discriminant).ti,ab, (interscale AND correlation*).ti,ab, error*.ti,ab, "individual variability".ti,ab, ((variability AND (analysis OR values))).ti,ab, ((uncertainty AND (measurement OR measuring))).ti,ab, "standard error of measurement".ti,ab, sensitiv*.ti,ab, responsiv*.ti,ab, (((minimal OR minimally OR clinical OR clinically) AND (important OR significant OR detectable) AND (change OR difference))).ti,ab, (meaningful AND change).ti,ab, "ceiling effect".ti,ab, "floor effect".ti,ab, "item response model".ti,ab, IRT.ti,ab, rasch.ti,ab, "differential item functioning".ti,ab, DIF.ti,ab, "computer adaptive testing".ti,ab, "item bank".ti,ab, "cross-cultural equivalence".ti,ab, "performance based tests".ti,ab **(OR)**

Search strategy

#1 Construct search (OR)

#2 Instrument search (OR)

#3 Population search (OR)

#4 filter for measurement properties (OR)

(#1 AND #3) AND (#2 OR #4 AND #3)

3.4.2 Eligibility criteria

3.4.2.1 Inclusion criteria

The following inclusion criteria were applied: (a) adults aged over 18 years with gout, (b) assessment of HRQOL or evaluation of the clinimetric properties of one or more instruments, and (c) publication in English. Both primary care and secondary care studies were included.

3.4.2.2 Exclusion criteria

Publications without empirical data (such as commentaries, editorials, reviews), randomized controlled trials deemed to be non-representative of a 'typical' population with gout and articles not available as full-text were excluded. Articles in French (4), Russian (2), German (1) and Spanish (1) were also excluded as the two reviewers (Priyanka Chandratre, PC and Lorna Clarson, LC) were unable to translate these into English.

3.4.2.3 Study selection

Titles and abstracts of identified articles were independently reviewed against the criteria above by two reviewers (PC, LC). Articles that could not be excluded based on title and abstract screening alone were included for full-text review, carried out independently by the same two reviewers. Further exclusions were made based on re-application of the inclusion and exclusion criteria. The reference lists of all full-text papers were examined for relevant studies. Disagreements at all stages were arbitrated through consensus meetings.

3.4.2.4 Data extraction

The following data were extracted independently by the two reviewers (PC and LC): study design (length and method of recruitment, inclusion and exclusion criteria, controls), participants (sample size, geographic location, setting, mean age, gender, ethnicity, method of gout diagnosis),

study response rate or attrition, methods of measurement (follow-up, statistical analysis), HRQOL scores and factors associated with poor HRQOL. For studies presenting HRQOL scores and their associates, data extraction form based on the Newcastle Ottawa Scale was used (Wells, Shea et al. 2000). Consensus-based standards for the selection of health measurement instruments (COSMIN) checklist was used as a guide to developing the data extraction form for the studies focusing on the clinimetric properties of questionnaires (Mokkink, Terwee et al. 2010). Data extracted to rate study methodology (cross-sectional, cohort and qualitative) are presented in appendix 4. Data extracted from studies that report clinimetric values are presented within this chapter (see Table 3-7).

3.4.3 Methodological Assessment

3.4.3.1 Clinimetric properties

The quality of the following clinimetric properties of HRQOL instruments was assessed by both reviewers (PC and LC) against a modified version of the quality criteria for measurement properties by Terwee et al (Terwee, Bot et al. 2007) as shown in Table 3-2:- validity (content, known group, floor or ceiling effects, construct and concurrent), reliability (internal consistency and test-retest) and responsiveness. Modification were made to the original quality criteria (Terwee, Bot et al. 2007) based on commonly found concepts or measurement properties in a preliminary review of the articles by the first reviewer (PC). Some quality criteria suggested by Terwee et al (Terwee, Bot et al. 2007) found to be of no or minimal relevance to the identified articles were omitted from the modified criteria in Table 3-2. Content validity in this review focuses on the target population (those with gout) and expert involvement. In addition known group validity has been added to acknowledge hypotheses a priori in the context of other disease characteristics. Factor analysis is used to determine whether items form one or more scales (Terwee, Bot et al. 2007). However it was the consistency of the items within a scale that was of

key interest in most of the identified articles hence Cronbach's alpha was used instead in the modified criteria. A value between 0.70 and 0.95 is considered a measure of good internal consistency (Terwee, Bot et al. 2007). Highest and lowest values for Cronbach's (and Interclass Correlation Coefficient, ICC) were used as there were multiple studies reporting the measurement properties of a single questionnaire. The scores of a questionnaire were assessed against the scores of a pre-existing gold standard, or criterion validity. Although the original quality criteria used 0.7 as a cut-off for acceptable correlation, the modified version includes correlations <0.5 and 0.5 to 0.7 as an additional quality criteria to differentiate between poor, moderate and good correlations. In the absence of a gold standard, construct validity was judged by correlation with clinical characteristics or known group validity (Hirsch, Lee et al. 2008). Construct validity criteria using the Pearson's correlation coefficient were defined as follows: <0.30 small, 0.30 to 0.50 moderate and > 0.50 large (Cohen, Cohen et al. 2013). Agreement was not assessed as majority of the identified studies did not repeat HRQOL measurements. In addition to the tests for responsiveness specified in the original quality criteria, effect size was also included with the following cut-off points as per Cohen's criteria (Cohen 1992): 0 to 0.19 negligible, 0.20-0.49 small, 0.50 to 0.79 moderate and ≥ 0.80 large. For floor and ceiling effects highest ratings were assigned to questionnaires with a value of $< 15\%$ for both (instead of one or the other as specified in the original quality criteria).

Table 3-2: Modified quality criteria for the assessment of clinimetric properties of instruments used to measure HRQOL in gout

(Terwee, Bot et al. 2007)

Property	Quality criteria
Content validity	++Clear description of patient and expert involvement
	+ Clear description of either patient or expert involvement in item selection or expected known group validity
	- No patient or expert involvement or lower than expected known group validity
	0 no information found on target population involvement or known group validity
Internal consistency	++ Cronbach's alpha 0.70-0.95 for all subscales
	+ Cronbach's alpha subscale lowest value <0.70 but highest value >0.70
	- Cronbach's alpha subscale highest value <0.70 or >0.95
	0 No information on internal consistency
Criterion validity	++ Correlation with gold standard >0.70
	+Correlation with gold standard between 0.5 and 0.7
	- Correlation with gold standard <0.5
	0 no information on criterion validity
Construct validity	++ Specific hypotheses a priori AND correlation with specified variable >0.50
	+ Correlation with specified variable between 0.3-0.5
	- Correlation with specified variable <0.3

Property	Quality criteria
	0 No hypothesis
Test retest reliability	++ ICC or weighted Kappa for all subscales >0.70
	+ ICC or weighted Kappa lowest value<0.70 but highest value >0.70
	- ICC or weighted Kappa highest value <0.70
	0 no information on reliability
Responsiveness	++ SDC or SDC <MIC OR MIC outside LOA OR Guyatt's RR>1.96 OR AUC >0.70
	+ ES >0.5 or >20% change in the expected direction
	- SDC or SDC >MIC Or MIC equals or inside LOA OR Guyatt's RR <1.96 OR AUC <0.70 despite adequate designs or methods, ES <0.5 or < 20% change
	0 No information on responsiveness
Floor and ceiling effects	+ <15% of respondents achieve highest and lowest scores
	+ <15% of respondents achieve highest or lowest scores
	- >15% respondents achieve highest or lowest scores despite robust methods or designs
	0 No information about floor ceiling effects

Key to ratings: ++ clear evidence, + some evidence, - poor evidence, 0 no information available.

Abbreviations: MIC: minimally important change; SDC: smallest detectable change; LOA: limits of agreement; ICC: intraclass correlation; RR: Responsiveness ratio; AUC: area under curve; ES: effect size

3.4.3.2 Quality assessment of studies with empirical HRQOL scores

Critical appraisal is defined as:

“The process of systematically examining research evidence to assess its validity, results and relevance before using it to inform a decision” (Hill, Spittlehouse 2001, p.1)

Cohort studies were assessed against the standards set by the Newcastle Ottawa Scale (NOS) for assessing the quality of non-randomised studies (Wells, Shea et al. 2000). Studies were assessed on selection (representativeness of the cohort, source of controls, predictors of HRQOL and method of diagnosis of gout), comparability (matching of controls for age and gender, difference in HRQOL between the two groups) and outcome (length of follow-up and attrition rates, triangulation of HRQOL scores against medical records). Assessment of the methodological quality of cross-sectional studies included the following modifications to the original NOS scale: baseline associates of HRQOL, response rate and a measure of association between poor HRQOL in gout compared to controls. Qualitative studies were assessed against the criteria set by the ‘Critical Appraisal Skills Programme’ (CASP) (Singh 2013). This instrument has been endorsed by the ‘Guidance for Inclusion of Qualitative Research in Cochrane Systematic Reviews of Interventions’ (Noyes, Booth et al. 2011) and is applicable to all qualitative research regardless of the methodology used to conduct it. It contains 10 items which are self-explanatory and suited to researchers with little experience of using qualitative studies in systematic reviews. These included the justification of using a qualitative approach, appropriateness of the research design and data collection in the context of the research question, recruitment strategies, the impact of the relationship between the researcher and the participants and consideration of ethical issues

3.5 Results

3.5.1 Study Selection

761 potentially relevant articles were identified: 474 articles were included in title and abstract screening after removal of duplicated papers. 450 articles were excluded during the title and abstract screening stages, leaving 24 to be included for full-text review. After full-text review of the remaining 24 articles as well as a further 5 articles identified from reference lists, 22 articles met the inclusion criteria. Reasons for exclusion are described in figure 2. For studies included in the review, the design, population source, sample size, study period, geographical location, year of publication and questionnaire(s) used to measure HRQOL are summarized in Table 3-3

Figure 2: Systematic Search and study selection

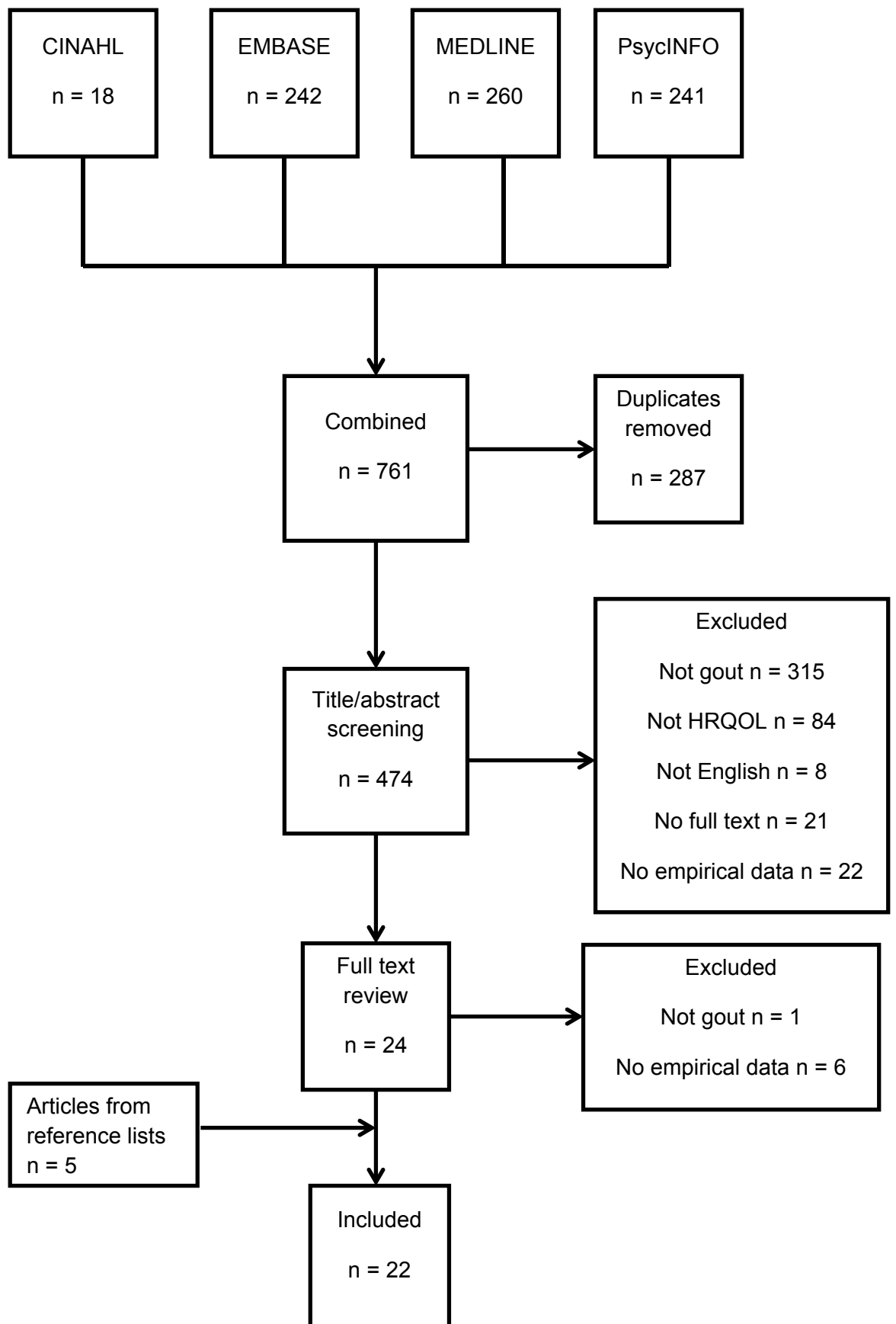


Table 3-3: Characteristics of studies providing data on HRQOL in Gout

1 st Author	Study Period	Publication Year	Location	Source of data / recruitment	Study type	Sample size	HRQOL measure
Singh, Strand 2008	1996-1998	2008	USA	Veterans Affairs database	Cross-sectional	70,334	SF-36 (veterans)
Colwell, Hunt et al. 2006	NR	2006	USA	Phase 2 clinical trial of Febuxostat	Nested prospective cohort	126	GAQ 1.0
Taylor, Colvine et al. 2008	NR	2008	New Zealand	Study of hand function in gout and Rheumatology clinics	Cross-sectional	73	HAQ-DI
Hirsch, Terkeltaub et al. 2010	NR	2010	USA	Multi-specialty clinics (physician, poster and newspaper advert recruitment)	Cross-sectional	371	GIS
Hirsch, Lee et al. 2008	NR	2008	USA	Multi-specialty clinics (physician, poster and newspaper advert recruitment)	Cross-sectional	371	GIS
Roddy, Zhang et al. 2007c	NR	2007	UK	Two GP practices	Cross-sectional	13,684	WHOQOL-BREF
Dalbeth, Taylor et al. 2009	NR	2011	New Zealand	Advertisements in the community and secondary care clinics	Prospective cohort	142	BIPQ, HAQ II
Alvarez-Hernandez, Zamudio-Lerma et al. 2009	NR	2009	Spain	Not described	Prospective cohort	49	AIMS, MOS 20
Lee, Hirsch et al. 2009	NR	2009	USA	Advertisements in primary and secondary care clinics	Cross-sectional	371	SF-36

1 st Author	Study Period	Publication Year	Location	Source of data / recruitment	Study type	Sample size	HRQOL measure
Sarkin, Levack et al. 2010	NR	2010	USA	Advertisements in community clinics and newspapers	Cross-sectional	260	GIS
Becker, Schumacher et al. 2009	NR	2009	USA	Academic and private rheumatology clinics	Prospective cohort	110	SF-36 and HAQ-DI
Ten Klooster, Oude Voshaar et al. 2011	2005-2008	2011	Netherlands	Out-patient rheumatology clinics	Cross-sectional	102	HAQ-DI, HAQ II and SF-36-PF-10
Khanna, Ahmed et al. 2008	NR	2008	USA	Private clinic and University of Cincinnati, Veterans Affairs Medical Center	Cross-sectional	80	SF-36, EQ5D and HAQ-DI
Alvarez-Hernandez, Pelaez-Ballesteros et al. 2008	NR	2008	Mexico	Eight rheumatology departments	Prospective cohort	206	HAQ-DI
Khanna, Perez-Ruiz et al. 2011	NR	2011	Spain	Gout clinic	Prospective cohort	99	SF-36
Lindsay, Gow et al. 2011	NR	2011	New Zealand	Primary and secondary care clinics	Qualitative Interviews	11	None
Khanna, Sarkin et al. 2011	NR	2011	USA	RCT of Rilonacept vs placebo	Nested prospective cohort	73	GIS
Groen, Klooster et al. 2010	2005 – 2008	2010	Netherlands	Outpatient Rheumatology clinic	Cross-sectional	102	HAQ-DI
Alvarez-Nemegyei, Cen-Piste et al. 2005	1999	2005	Mexico	Primary care	Nested case-control in a cohort	90	HAQ
Harrold, Mazor et al. 2010	2005-2010	2010	USA	Multi-specialty practice (Fallon clinic)	Qualitative	26	None

1 st Author	Study Period	Publication Year	Location	Source of data / recruitment	Study type	Sample size	HRQOL measure
Singh, Sarkin et al. 2011	NR	2011	USA	Multi-specialty clinics (physician, poster and newspaper advert recruitment)	Cross-sectional	298	Healthcare utilization frequency
Khanna, Nuki et al. 2012	2010	2012	USA, UK, Germany, France	National Health and Wellness Survey, Lightspeed Research panel	Cross-sectional	1936	SF12 v2, SF-6D

Abbreviations: MOS 20: Medical Outcomes Survey 20; AIMS: Arthritis Impact Measurement Scales; SF-36: Short Form 36; PF-10: Physical Function 10 of the SF-36; HAQ-DI: Health Assessment Questionnaire Disability Index; HAQ II: Health Assessment Questionnaire II; GAQ 1.0: Gout Assessment Questionnaire 1.0; GIS: Gout Impact Scale; WHO QOL BREF: World Health Organisation Quality of Life brief version; BIPQ: Brief Illness Perception Questionnaire; SF12v2: Short Form 12 version 2; SF6D: Short Form 6D; EQ5D: EuroQol 5D; NR: not reported; RCT: randomized controlled trial; UK: United Kingdom; USA: United States of America.

3.5.2 Study characteristics and methodological quality

Of the 22 included studies, 8 evaluated the clinimetric properties of instruments used to measure HRQOL: (Taylor, Colvine et al. 2008; Colwell, Hunt et al. 2006; Alvarez-Hernandez, Pelaez-Ballestas et al. 2008; Alvarez-Hernandez, Zamudio-Lerma et al. 2009; Khanna, Perez-Ruiz et al. 2011; Ten Klooster, Oude Voshaar et al. 2011; Khanna, Sarkin et al. 2011; Hirsch, Lee et al. 2008) and the remainder focused on self-reported HRQOL or healthcare utilization (Singh, Strand 2008; Roddy, Zhang et al. 2007c; Lee, Hirsch et al. 2009; Khanna, Ahmed et al. 2008; Hirsch, Terkeltaub et al. 2010; Dalbeth, Petrie et al. 2011; Sarkin, Levack et al. 2010; Lindsay, Gow et al. 2011; Groen, Klooster et al. 2010; Alvarez-Nemegyei, Cen-Piste et al. 2005; Harrold, Mazor et al. 2010; Singh, Sarkin et al. 2011; Khanna, Nuki et al. 2012). One study reported both the measurement properties as well as the scores of HRQOL as measured by the HAQ-DI and SF-36. (Becker, Schumacher et al. 2009). All studies were published in or after 2006. Thirteen cross-sectional (Singh, Strand 2008; Roddy, Zhang et al. 2007c; Taylor, Colvine et al. 2008; Ten Klooster, Oude Voshaar et al. 2011; Lee, Hirsch et al. 2009; Khanna, Ahmed et al. 2008; Hirsch, Terkeltaub et al. 2010; Hirsch, Lee et al. 2008; Sarkin, Levack et al. 2010; Groen, Klooster et al. 2010; Alvarez-Nemegyei, Cen-Piste et al. 2005; Singh, Sarkin et al. 2011; Khanna, Nuki et al. 2012), seven cohort (Colwell, Hunt et al. 2006; Becker, Schumacher et al. 2009; Alvarez-Hernandez, Pelaez-Ballestas et al. 2008; Alvarez-Hernandez, Zamudio-Lerma et al. 2009; Khanna, Sarkin et al. 2011; Khanna, Perez-Ruiz et al. 2011; Dalbeth, Petrie et al. 2011) and two qualitative studies (Lindsay, Gow et al. 2011; Harrold, Mazor et al. 2010) were identified. The median sample size of the twenty quantitative studies was 134 (range 49-70,334). Only four studies (Becker, Schumacher et al. 2009; Khanna, Perez-Ruiz et al. 2011; Ten Klooster, Oude Voshaar et al. 2011; Lee, Hirsch et al. 2009) used the diagnostic 'gold standard' of MSU crystal identification from joint or tophus aspirate (Zhang, Doherty et al. 2006b). Other methods of gout diagnosis in studies included hyperuricaemia (n=3) (Colwell, Hunt et al. 2006; Ten Klooster, Oude Voshaar et al. 2011 and Khanna, Sarkin et al. 2011), American College of Rheumatology (ACR) classification criteria

(Wallace, Robinson et al. 1977) (n=11) (Taylor, Colvine et al. 2008; Alvarez-Hernandez, Pelaez-Ballestas et al. 2008; Alvarez-Hernandez, Zamudio-Lerma et al. 2009; Khanna, Ahmed et al. 2008; Dalbeth, Petrie et al. 2011; Hirsch, Lee et al. 2008; Sarkin, Levack et al. 2010; Lindsay, Gow et al. 2011; Groen, Klooster et al. 2010; Alvarez-Nemegyei, Cen-Piste et al. 2005 and Singh, Sarkin et al. 2011), self-reported gout (n=4) (Roddy, Zhang et al. 2007c; Khanna, Sarkin et al. 2011; Lee, Hirsch et al. 2009 and Khanna, Nuki et al. 2012), physician-diagnosis (n=2) (Lee, Hirsch et al. 2009 and Hirsch, Terkeltaub et al. 2010) and ICD-9 codes (n=1) (Singh, Strand 2008). Follow-up period in cohort studies ranged from 8 weeks (Alvarez-Hernandez, Zamudio-Lerma et al. 2009 and Khanna, Sarkin et al. 2011) to 2 years (Khanna, Perez-Ruiz et al. 2011). Five cross-sectional studies reported response rate of > 60% (Ten Klooster, Oude Voshaar et al. 2011; Lee, Hirsch et al. 2009; Hirsch, Terkeltaub et al. 2010; Hirsch, Lee et al. 2008 and Lindsay, Gow et al. 2011). The original NOS quality ratings are based on the award of a maximum of one star for each numbered item within the selection and outcome categories and two stars for comparability (Wells, Shea et al. 2000). The modified NOS quality ratings in this review are defined in Table 3-4. Quality assessment of cohort and cross-sectional studies presenting empirical data on HRQOL in gout is summarized in Table 3-5. Quality assessment of qualitative studies is summarized in Table 3-6

Table 3-4: Quality ratings for cohort and cross-sectional studies presenting empirical data on HRQOL in gout

Category	Rating per item
Selection	+ Cohort truly or somewhat representative of a gout population
	- Selected cases only
	NR No description of the derivation of sample
	+ Controls from the same source as cases
	- Controls from a different source to cases
	NR No description of the derivation of controls
	+ Effect estimates (relative risk, odds ratio or correlation coefficient) presented for associates (cross-sectional) or predictors (cohort) of HRQOL
	- No effect estimates given
	NR No description of derivation of effect estimates
	+ Diagnosis of gout using crystal identification, ARA criteria or record linkage
	- Diagnosis of gout not based on above methods
	NR No description of how gout was diagnosed
Comparability	+ Age and sex matched controls
	- Controls unmatched for age and sex

Category	Rating per item
	NR No description of matching controls to cases
	+ Measure of association (relative risk or odds ratio) with HRQOL presented for cases and controls
	- Measure of association not presented for cases and controls
	NR No description of a measure of association
Outcome	+ HRQOL triangulation with objective assessment (physician, medical records)
	- HRQOL not triangulated with other sources
	NR No description of whether HRQOL triangulated with other sources
	+ Adequate follow-up period (≥ 12 months) (cohort studies only)
	- Follow-up period not adequate
	NR No description of follow-up period
	+ Response rate (RR) $> 60\%$ (cross-sectional studies only) or attrition $< 30\%$ (cohort studies only)
	- RR $< 60\%$ or attrition $> 30\%$
	NR No description of RR or attrition

Abbreviations: NR: Not Recorded; RR: Response Rate; ARA: American Rheumatism Association; HRQOL: Health Related Quality of Life

Table 3-5: Modified NOS criteria for the methodological assessment of cohort and cross-sectional studies

Study Details		Selection			Comparability			Outcome	
	Cohort representative of average gout patient in community	Controls from same source as cases	HRQOL associations (CS) or predictors/change (Cht)	Diagnosis of gout: MSU crystals, ARA criteria (Wallace, Robinson et al. 1977) or record linkage	Controls matched for age/gender	Measure of association (OR or RR)	HRQOL triangulated with independent physician assessment, secure records or record linkage	Adequate follow-up period (Cht only)	Response rate >60% (CS) or attrition <30% (Cht)
Cross-sectional studies (CS)									
Singh, Strand 2008	+	+	+	+	-	NR	+	Not relevant	-
Hirsch, Terkeltaub et al. 2010	+	NR	+	+	NR	NR	+	Not relevant	+
Hirsch, Lee et al. 2008	+	NR	+	+	NR	NR	+	Not relevant	+
Roddy, Zhang et al. 2007c	-	+	+	-	-	NR	+	Not relevant	-
Lee, Hirsch et al. 2009	+	+	+	+	+	NR	+	Not relevant	+
Sarkin,	+	NR	+	+	NR	NR	+	Not	NR

Study Details		Selection			Comparability			Outcome	
	Cohort representative of average gout patient in community	Controls from same source as cases	HRQOL associations (CS) or predictors/change (Cht)	Diagnosis of gout: MSU crystals, ARA criteria (Wallace, Robinson et al. 1977) or record linkage	Controls matched for age/gender	Measure of association (OR or RR)	HRQOL triangulated with independent physician assessment, secure records or record linkage	Adequate follow-up period (Cht only)	Response rate >60% (CS) or attrition <30% (Cht)
	Levack et al. 2010							relevant	
	Ten Klooster, Oude Voshaar et al. 2011	-	NR	-	+	NR	NR	-	Not relevant +
	Khanna, Ahmed et al. 2008	-	NR	+	+	NR	NR	+	Not relevant NR
	Taylor, Colvine et al. 2008	-	NR	+	+	NR	NR	-	Not relevant NR
	Groen, Klooster et al. 2010	-	+	NR	+	-	NR	-	Not relevant NR
	Alvarez-Nemegyei,	+	+	+	+	-	+	+	Not NR

Study Details		Selection			Comparability			Outcome	
	Cohort representative of average gout patient in community	Controls from same source as cases	HRQOL associations (CS) or predictors/change (Cht)	Diagnosis of gout: MSU crystals, ARA criteria (Wallace, Robinson et al. 1977) or record linkage	Controls matched for age/gender	Measure of association (OR or RR)	HRQOL triangulated with independent physician assessment, secure records or record linkage	Adequate follow-up period (Cht only)	Response rate >60% (CS) or attrition <30% (Cht)
	Cen-Piste et al. 2005							relevant	
	Singh, Sarkin et al. 2011	+	NR	+	+	NR	+	+	Not relevant
	Khanna, Nuki et al. 2012	+	NR	+	-	NR	+	-	Not relevant
Cohort studies (Cht)									
	Colwell, Hunt et al. 2006	-	NR	+	-	NR	NR	+	+
	Dalbeth, Petrie et al. 2011	+	NR	+	+	NR	NR	+	+
	Alvarez-Hernandez, Zamudio-Lerma et al.	-	NR	+	+	NR	NR	+	-

Study Details		Selection			Comparability			Outcome	
	Cohort representative of average gout patient in community	Controls from same source as cases	HRQOL associations (CS) or predictors/change (Cht)	Diagnosis of gout: MSU crystals, ARA criteria (Wallace, Robinson et al. 1977) or record linkage	Controls matched for age/gender	Measure of association (OR or RR)	HRQOL triangulated with independent physician assessment, secure records or record linkage	Adequate follow-up period (Cht only)	Response rate >60% (CS) or attrition <30% (Cht)
2009									
Becker, Schumacher et al. 2009	-	NR	+	+	NR	NR	+	+	-
Alvarez-Hernandez, Pelaez-Ballestas et al. 2008	+	NR	+	+	NR	NR	+	+	+
Khanna, Perez-Ruiz et al. 2011	-	NR	+	+	NR	NR	+	+	-
Khanna, Sarkin et al. 2011	-	NR	+	-	NR	NR	-	-	+
Abbreviations: +: positive rating; -: negative rating; ARA: American Rheumatism Association; Cht: cohort study; CS: cross-sectional study; MSU: monosodium urate; NR: not reported; OR: odds ratio; RR: relative risk									

Table 3-6: CASP Quality appraisal for qualitative studies

Study ID	Lindsay, Gow et al. 2011	Harrold, Mazor et al. 2010
Was the use of qualitative methodology justified?	Yes	Yes
Was the research design appropriate to address the aims of the research?	Yes	Yes
Was the recruitment strategy appropriate to the aims of the research?	Lack of information regarding non-participants	Yes
Were the data collected in a way that addressed the research question?	Yes	Yes
Has the relationship between researcher and participants been considered?	Yes	Yes
Have ethical issues been taken into consideration?	Yes	No
Was data analysis sufficiently rigorous?	Contradictory data and researcher's role, potential for bias and influence during data analysis not reported	Yes
Is there a clear statement of findings?	Yes	Yes
How valuable is the research?	Yes	Yes

3.5.3 Instruments used to measure HRQOL in gout

Twelve different instruments to measure HRQOL were identified (5 studies employed more than one instrument) (Becker, Schumacher et al. 2009; Alvarez-Hernandez, Zamudio-Lerma et al. 2009; Ten Klooster, Oude Voshaar et al. 2011; Khanna, Ahmed et al. 2008 and Dalbeth, Petrie et al. 2011). Most commonly-used were the Health Assessment Questionnaire Disability Index (HAQ-DI, n=6) (Taylor, Colvine et al. 2008; Becker, Schumacher et al. 2009; Alvarez-Hernandez, Pelaez-Ballestas et al. 2008; Ten Klooster, Oude Voshaar et al. 2011; Khanna, Ahmed et al. 2008 and Groen, Klooster et al. 2010), Short Form 36 (SF-36, n=5) (Singh, Strand 2008; Becker, Schumacher et al. 2009; Khanna, Perez-Ruiz et al. 2011; Lee, Hirsch et al. 2009 and Khanna, Ahmed et al. 2008), Gout Impact Scale (GIS, n=4) (Khanna, Sarkin et al. 2011; Hirsch, Terkeltaub et al. 2010; Hirsch, Lee et al. 2008 and Sarkin, Levack et al. 2010) and Health Assessment Questionnaire II (HAQ II, n=2) (Ten Klooster, Oude Voshaar et al. 2011 and Dalbeth, Petrie et al. 2011). The Gout Assessment Questionnaire 1.0 (GAQ 1.0) (Colwell, Hunt et al. 2006), Arthritis Impact Measurement Scale (AIMS) (Alvarez-Hernandez, Zamudio-Lerma et al. 2009), Medical Outcomes Survey 20 (MOS 20) (Alvarez-Hernandez, Zamudio-Lerma et al. 2009), Brief Illness Perception Questionnaire (BIPQ) (Dalbeth, Petrie et al. 2011), SF-36 Physical Function 10 (PF-10) (Ten Klooster, Oude Voshaar et al. 2011), Short Form 12 (SF12v2) (Khanna, Nuki et al. 2012), Health Assessment Questionnaire (HAQ) (Alvarez-Nemegyei, Cen-Piste et al. 2005), EuroQOL 5D (EQ5D) (Khanna, Ahmed et al. 2008), Short Form 6D (SF6D) (Khanna, Nuki et al. 2012) and World Health Organisation Quality of Life (WHOQOL) bref (Roddy, Zhang et al. 2007c) were each used once.

3.5.4 Clinimetric properties of instruments used to measure HRQOL in gout

The available values of the measurement properties of instruments are presented in Table 3-7 and ratings assigned to the instruments are summarized in Table 3-8.

Table 3-7: Measurement values of instruments used to measure HRQOL

Measurement instrument	Reliability		Validity				Responsiveness
	Internal Consistency (Cronbach's Alpha)	Test retest (ICC)	Content	Construct (Pearson or Spearman's r)	Concurrent (Pearson or Spearman's r)	Hypothesis a priori	MCID, SDC, ES, Guyatt's RR or >20% change in scores
GIS (Khanna, Sarkin et al. 2011; Hirsch, Lee et al. 2008)	0.54 - 0.94	0.77-0.89	Patients and rheumatologists	Patient severity (r= 0.31 to 0.45), attack freq. (r=0.06 to 0.51), attack pain (r= 0.13 to 0.47), physician severity (r= 0.02 to 0.34) PCS (r= -0.10 to -0.20). MCS r= -0.17 to -0.43	NR	Yes	ES 0.218 – 0.376 in the minimally improved and 0.129 – 0.682 in the markedly improved groups
GAQ 1.0 (Colwell, Hunt et al. 2006)	0.78-0.97	NR	Patients and Rheumatologists	PCS r= 0.02 to 0.34. MCS r= -0.01 to 0.23. MOS r= 0.03 to 0.46	NR	Yes	GRR 0.03 (1 month) to 1.14 (6 months). MCID 1.88 to 12.33 (not significant in well being for pain freq.)
HAQ-DI (Taylor, Colvine et al. 2008; Becker, Schumacher et al. 2009; Alvarez-	0.81 - 0.97	0.68 – 0.84	Floor 20.5%, Ceiling 34%	Freq. of attacks r = 0.41, physician global r= 0.42 - 0.77, Swollen joints r= 0.40 – 0.62, painful joints	SF-36 r= -0.44 to -0.83, PCS r= -0.71 MCS r= -0.56,	Yes (55.5% true)	Mean ES = 0.62 (moderate), SDC =0.59 and GRR= 1.91

Measurement instrument	Reliability		Validity			Responsiveness	
	Internal Consistency (Cronbach's Alpha)	Test retest (ICC)	Content	Construct (Pearson or Spearman's r)	Concurrent (Pearson or Spearman's r)	Hypothesis a priori	MCID, SDC, ES, Guyatt's RR or >20% change in scores
Hernandez, Pelaez-Ballestas et al. 2008; Ten Klooster, Oude Voshaar et al. 2011)				r= 0.46 - 0.650, joints with limited mobility r= 0.36, VAS pain r= 0.56, tophi r= 0.42, Excellent /very good health = 0.16, good= 0.33, fair/poor= 1.25	DASH r= 0.81, Sollerman r= - 0.79, ACR functional class r= 0.79, HAQII r= 0.87, PF-10 r= - 0.75		
SF-36 (Becker, Schumacher et al. 2009; Khanna, Perez-Ruiz et al. 2011)	0.75 – 0.97	0.40 - 0.90	Ceiling RP =18.4%, SF= 32.7%, RE= 58.6%	PCS: tophi r=0.277, swollen joints r=-0.334, painful joints r= -0.544, attacks last year r=-0.369, MCS: painful joints r= - 0.436, freq. of attacks r=- 0.321	NR	NR	Colchicine: ES for PCS = 0.3 (small) ES for MCS= 0.16 (negligible) Colchicine + ULT: ES for PCS =0.99 (large) ES for MCS= 0.08 (negligible)

Measurement instrument	Reliability		Validity				Responsiveness
	Internal Consistency (Cronbach's Alpha)	Test retest (ICC)	Content	Construct (Pearson or Spearman's r)	Concurrent (Pearson or Spearman's r)	Hypothesis a priori	MCID, SDC, ES, Guyatt's RR or >20% change in scores
							MCID (all subjects) 70% for PCS and 38% in MCS
MOS 20 (Alvarez-Hernandez, Zamudio-Lerma et al. 2009)	0.68-1.0	0.27-0.65.	NR	JFL: 23.75 to 66 Without JFL: 37.59 to 81.43	HAQ-DI r = -0.1 to -0.5	NR	>20% change - PF, SF, health perception, pain,
AIMS (Alvarez-Hernandez, Zamudio-Lerma et al. 2009)	0.66- 0.96	0.11-0.70	NR	JFL: 3.05 to 6.62 Without JFL: 1.99 to 5.46	HAQ-DI r= 0.1 to 0.6	NR	>20% change - dexterity, daily activity, social development, pain, depression
HAQII (Ten Klooster, Oude Voshaar et al. 2011)	0.94	NR	Ceiling 25.8%	Excellent/very good health = 0.28, good= 0.44, fair/poor= 1.39	PF-10 r= -0.79. SF-36 -0.35 (MH) to 0.72 (RP)	Yes	NR
PF-10 (Ten Klooster, Oude Voshaar et al. 2011)	0.94	NR	NR	Excellent/very good health= 71.91, good =74.27,fair/poor= 39.33	HAQ-DI r= -0.75. SF-36 0.30 (MH) to 0.68 (RP)	Yes	NR

Abbreviations: MCID: minimal clinically important difference; SDC: smallest detectable change; ES: Effect size; GRR: Guyatt's responsiveness ratio; NR:

Measurement instrument	Reliability		Validity			Responsiveness	
	Internal Consistency (Cronbach's Alpha)	Test retest (ICC)	Content	Construct (Pearson or Spearman's r)	Concurrent (Pearson or Spearman's r)	Hypothesis a priori	MCID, SDC, ES, Guyatt's RR or >20% change in scores

not reported; JFL: joints with functional limitations; VAS: visual analogue score; SF-36 subscales: PCS: physical component summary, MCS: mental component summary, RP: role physical, MH: mental health, SF: social function, RE: role emotional; freq.: frequency, ICC: Interclass Correlation Coefficient; GIS: Gout Impact Scale; HAQ-DI: Health Assessment Questionnaire Disability Index; HAQ II: Health Assessment Questionnaire II; MOS 20: Medical Outcomes Survey 20; PF-10: Physical Function 10; AIMS: Arthritis Impact Measurement Scale; GAQ 1.0: Gout Assessment Questionnaire; SF-36: Short-Form 36; DASH: Disability of the Arm, Shoulder and Hand.

Table 3-8: Ratings assigned to the measurement properties of the identified instruments

Instrument	Content validity	Floor or ceiling effects	Construct Validity	Concurrent validity	Internal consistency	Test- retest reliability	Responsiveness
GIS	++	0	+	-	+	++	+
GAQ	++	0	+	0	++	0	-
HAQ-DI	+	-	++	++	++	++	+
HAQ II	+	-	++	++	++	0	0
SF-36	0	-	+	0	++	+	+
MOS 20	+	0	0	-	+	-	+
PF-10	-	0	+	++	++	0	0
AIMS	+	0	0	+	+	-	+

Key to ratings: ++ clear evidence, + some evidence, - poor evidence, 0 no information available.

Abbreviations: GIS: Gout Impact Scale; HAQ-DI: Health Assessment Questionnaire Disability Index; HAQ II: Health Assessment Questionnaire II; MOS 20: Medical Outcomes Survey 20; PF-10: Physical Function 10; AIMS: Arthritis Impact Measurement Scale; GAQ 1.0: Gout Assessment Questionnaire; SF-36: Short-Form 36

3.5.5 Summary of clinimetric properties of the instruments

Content validity was only established for the gout-specific GIS and GAQ 1.0 which received patient and healthcare provider input during the development of the questionnaires (Colwell, Hunt et al. 2006; Hirsch, Lee et al. 2008). The generic SF-36 (except PF-10 (Ten Klooster, Oude Voshaar et al. 2011)) and the HAQ-DI (Taylor, Colvine et al. 2008; Becker, Schumacher et al. 2009; Alvarez-Hernandez, Pelaez-Ballestas et al. 2008; Alvarez-Hernandez, Zamudio-Lerma et al. 2009; Khanna, Perez-Ruiz et al. 2011) performed well in the known-group analysis based on self-reported general health, co-morbidities and correlation with disease characteristics. The HAQ-DI, HAQII and SF-36 had significant floor (HAQ-DI 20.5%) and ceiling (HAQ-DI 34%, HAQII 25.8%, SF-36 18.4%) effects, indicating a weakness in the ability to differentiate between participants at the extreme ends of the scale (no disability and severe disability) leading to limited content validity and responsiveness to change (Taylor, Colvine et al. 2008; Khanna, Perez-Ruiz et al. 2011). The GIS showed poor construct validity with low correlations between the subscales of GIS (except unmet treatment need) and physician-rated severity ($r=0.02$ to 0.34) although moderate correlations were seen with patient-rated severity ($r=0.31$ to 0.45) (Khanna, Sarkin et al. 2011; Hirsch, Lee et al. 2008). Correlations of the SF-36 Mental Component Summary (MCS) ($r=-0.17$ to -0.43) with the GIS were generally higher than those seen with the Physical Component Summary (PCS) ($r=-0.10$ to -0.20) (NB correlation coefficients are negative as higher scores indicate better health status on the SF-36 but worse health status on the GIS (Terkeltaub 2011)). The GAQ 1.0 had better correlation with the MOS health distress questionnaire ($r=0.03$ to 0.46) than the SF-36 (PCS $r=0.02$ to 0.34 , MCS $r=-0.01$ to 0.23) (Colwell, Hunt et al. 2006). The HAQ-DI and HAQII had excellent correlation with each other ($r=0.87$) as well as the SF-36 (HAQ-DI $r=-0.41$ to -0.83 , HAQII $r=-0.35$ to 0.72) (Alvarez-Hernandez, Pelaez-Ballestas et al. 2008; Ten Klooster, Oude Voshaar et al. 2011).

Most instruments had good or excellent internal consistency (Cronbach's α 0.4 to 1.0), except the GIS (weak correlation between items of the gout medication side-effects and unmet treatment needs) (Hirsch, Lee et al. 2008). Test-retest reliability was low for the AIMS (intra-class correlation coefficient (ICC) 0.11 to 0.70) and the MOS 20 (ICC 0.27 to 0.65) (Alvarez-Hernandez, Zamudio-Lerma et al. 2009) but acceptable for the HAQ-DI (ICC 0.68 to 0.84) (Alvarez-Hernandez, Pelaez-Ballestas et al. 2008). Responsiveness to clinical change was elicited by the Minimal Clinically Important Difference (MCID) of 5 to 8 points for the subscales of the GIS (Khanna, Sarkin et al. 2011), SF-36 (Khanna, Perez-Ruiz et al. 2011) and GAQ 1.0 (in all subscales except wellbeing anchored to pain frequency) (Colwell, Hunt et al. 2006) and 20% change in scores of the AIMS and MOS 20 (Alvarez-Hernandez, Zamudio-Lerma et al. 2009). Effect sizes (ES) of the PCS (SF-36) improved from small (0.3) in the treatment with colchicine only to large (0.99) in the ULT and colchicine group (Khanna, Perez-Ruiz et al. 2011). The magnitude of the ES was lower for the GIS (0.218 – 0.376 in the minimally improved and 0.129 – 0.682 in the markedly improved groups) (Khanna, Sarkin et al. 2011) and moderate (0.62) for the HAQ-DI (Alvarez-Hernandez, Pelaez-Ballestas et al. 2008).

3.5.6 The distribution of HRQOL in gout

No studies were identified that defined or used a specific cut-off value for poor HRQOL in gout. Higher scores indicate worse HRQOL in the GIS, GAQ 1.0, HAQ-DI, AIMS and BIPQ and better HRQOL in the WHOQOL-BREF and SF-36 (including PF-10, MOS 20 and SF12v2). Four studies identified instruments with scores lower than controls (SF-36 physical functioning, role-physical, bodily pain, general health, role emotional and PCS $p < 0.001$ (Singh, Strand 2008); WHOQOL-BREF $p = 0.003$ (Roddy, Zhang et al. 2007c)) and USA normative distribution (SF-36 PCS $p = 0.007$ (Lee, Hirsch et al. 2009), representative of poor HRQOL in gout (Singh, Strand 2008; Roddy, Zhang et al. 2007c; Lee, Hirsch et al. 2009 and Khanna, Nuki et al. 2012). One cohort study of 'treatment

failure gout' showed lower scores in all SF-36 domains (except mental health and Mental Component Summary (MCS)) compared to age and sex-matched US normative distribution (PCS and MCS normative distributions have a mean of 50 and standard deviation 10 for the US population) (Becker, Schumacher et al. 2009). One cohort (Khanna, Perez-Ruiz et al. 2011) and two cross-sectional studies (Roddy, Zhang et al. 2007c; Lee, Hirsch et al. 2009) highlighted the greater impact of gout on physical HRQOL (measured by the SF-36 (Khanna, Perez-Ruiz et al. 2011) and WHO-QOL BREF ($p<0.001$) (Roddy, Zhang et al. 2007c)) with a lesser reduction seen in the MCS compared to US norms ($p<0.001$) (Lee, Hirsch et al. 2009). However, the impact on physical function was mild as shown in two studies using the HAQ-DI, with a baseline HAQ-DI of 1 for those with treatment-failure gout (Becker, Schumacher et al. 2009) and 0.43 in chronic tophaceous gout (Alvarez-Hernandez, Zamudio-Lerma et al. 2009) (Consensus based cut-off for mild disability as measured by the HAQ-DI is a score <1 , moderate disability 1-2 and severe disability ≥ 2 (Krishnan, Tugwell et al. 2004)). Similarly the average HAQ score (surrogate for musculoskeletal disability) in another study was 0.17 (Alvarez-Nemegyei, Cen-Piste et al. 2005). Two cross-sectional studies (Groen, Klooster et al. 2010; Khanna, Nuki et al. 2012) comparing the impact of gout to other rheumatic diseases show substantially lower levels of disability (mean HAQ-DI 0.54) in patients with gout compared to those with rheumatoid arthritis (RA) (0.97) and osteoarthritis (1.00) (Groen, Klooster et al. 2010). Those with severe gout (≥ 3 attacks in the previous year and confirmed tophi) had similar health utility (SF6D) scores to patients with 'average' RA or systemic lupus (Khanna, Nuki et al. 2012). In two studies which utilized the GIS, participants' gout concern remained high despite their reporting finding treatment helpful (Khanna, Sarkin et al. 2011 and Hirsch, Terkeltaub et al. 2010) and in another cohort study using the generic BIPQ, the impact of gout was most severe on perceptions of chronicity (Dalbeth, Petrie et al. 2011). Gout severity was also associated with an increased utilisation of primary care clinics in a cross-sectional study of healthcare resources utilisation ($p=0.005$) (Singh, Sarkin et al. 2011)

3.5.6.1 Factors associated with poor HRQOL in gout

Co-morbidities

Hypertension was the most commonly reported co-morbidity (Hirsch, Terkeltaub et al. 2010; Hirsch, Lee et al. 2008). Two studies of physical functioning (measured by SF-36 and HAQ-DI) as an indicator of HRQOL and another study of healthcare utilization found that associated co-morbidities contribute to poorer HRQOL (PCS $r=-0.18$ to -0.43 , $p<0.01$ (Lee, Hirsch et al. 2009); HAQ-DI $p<0.03$ (Becker, Schumacher et al. 2009)) and higher number of primary care visits ($p=0.006$) (Singh, Sarkin et al. 2011). In one study of US veterans, co-morbidities were solely responsible for poor HRQOL, with no difference in HRQOL between those with and without gout after co-morbidities had been adjusted for (Singh, Strand 2008).

Gout characteristics

In a UK primary care-based cross-sectional study, the association between gout and poor physical HRQOL of the WHOQOL-BREF remained significant after adjustment for medical (diabetes, hypertension and chronic kidney disease) and musculoskeletal co-morbidities (WHOQOL-BREF $p=0.001$ (Roddy, Zhang et al. 2007c)). Cross-sectional association of gout characteristics (presence of tophi (PCS $p<0.01$, MCS $p<0.05$), uncertainty about the presence of tophi³ (PCS $p<0.001$, MCS $p<0.01$) and ≥ 4 attacks in the last 12 months (PCS $p<0.05$, MCS $p<0.05$)) with poor HRQOL and high activity impairment also remained significant even after adjustment for co-morbidities (Khanna, Nuki et al. 2012). In one cohort (Dalbeth, Petrie et al. 2011) and four cross-sectional studies (Lee, Hirsch et al. 2009; Hirsch, Lee et al. 2008; Alvarez-Nemegyei, Cen-Piste et al. 2005; Khanna, Nuki et al. 2012) gout-specific features (increasing frequency of attacks ($p=0.002$ (Lee, Hirsch et al. 2009), $p=0.044$ (Dalbeth, Petrie et al. 2011), $r=0.51$, $p<0.05$ (Khanna, Nuki et al. 2012)), time with pain between attacks ($p<0.001$ (Lee, Hirsch et al. 2009)), pain during a typical

³ Participants suspected having tophi but were unsure given the description used in the questionnaire ("deposits of crystallised uric acid that can appear as moveable lumps or whitish nodules") (Khanna, Nuki et al. 2012)

attack ($p=0.023$ (Lee, Hirsch et al. 2009)), number of joints involved in a typical attack ($p=0.004$ (Lee, Hirsch et al. 2009)), and presence of tophi (relative risk 4.3, 95% confidence interval (CI) 1.2-15.1 (Alvarez-Nemegyei, Cen-Piste et al. 2005); $p<0.05$ (Khanna, Nuki et al. 2012)) were reported to be associated with worse HRQOL (measured by the GIS, SF-36, SF12v2, HAQ and BIPQ) even after adjustment for age, gender, gout features and co-morbidities. Increased frequency of attacks in the previous year (≥ 3) (PCS $p<0.05$) and confirmed tophi (severe gout) (PCS $p<0.01$, MCS $p<0.01$) led to worse HRQOL compared to asymptomatic patients (Khanna, Nuki et al. 2012). The presence of tophi had a significant impact on activity impairment ($p<0.05$, (Khanna, Nuki et al. 2012)) and led to increased likelihood of consultation with a rheumatologist (odds ratio (OR) 7.92, 95%CI 2.81-22.34), $p<0.0001$ (Singh, Sarkin et al. 2011)) in two cross-sectional studies (Singh, Sarkin et al. 2011; Khanna, Nuki et al. 2012). Other cross-sectional variables such as physician-rated severity (primary care OR 1.46, 95%CI 1.02-2.08, $p=0.037$; rheumatologist OR 1.52, 95%CI 1.08-2.14, $p=0.018$), time since last gout attack (primary care OR 0.65, 95%CI 0.55-0.76, $p<0.0001$; rheumatologist OR 0.78, 95%CI 0.67-0.91, $p=0.001$) and an attack within the last 3 months (primary care OR 3.48, 95%CI 1.84-6.58, $p<0.0001$; rheumatologist OR 2.11, 95%CI 1.22-3.65, $p=0.008$) were also associated with healthcare resources utilization (Singh, Sarkin et al. 2011). Whilst some studies supported the association of tophi (GIS $p=0.029$ (Hirsch, Terkeltaub et al. 2010); PCS $p<0.01$, MCS $p<0.05$ (Khanna, Nuki et al. 2012)) and serum uric acid (SUA) ($p=0.002$) (Dalbeth, Petrie et al. 2011) with poor HRQOL, others did not (tophi: patient-severity rating $r=0.174$ (Sarkin, Levack et al. 2010); SUA: WHOQOL-BREF $p=0.750$ (Roddy, Zhang et al. 2007c), GIS $r<0.29$ (Hirsch, Terkeltaub et al. 2010), patient-severity rating $r=0.06$ (Sarkin, Levack et al. 2010). There was a paucity of cross-sectional evidence for positive effects of allopurinol on HRQOL from a patient's perspective (WHOQOL-BREF $p=0.618$ (Roddy, Zhang et al. 2007c), HAQ $p=0.79$ (Alvarez-Nemegyei, Cen-Piste et al. 2005)) whereas steroid and non-steroidal anti-inflammatory drugs were associated with greater musculoskeletal disability (Alvarez-Nemegyei, Cen-Piste et al. 2005). Although tophi, co-morbidities, polyarticular disease and radiographic damage were associated

with worse HRQOL at baseline, after multivariate analysis, reduction in attacks ($p=0.001-0.06$) and baseline SUA ($p=0.001-0.04$) were predictors of improvement in HRQOL in one cohort study (Khanna, Perez-Ruiz et al. 2011).

3.6 Discussion

Although none of the identified instruments to measure HRQOL in gout in this review were satisfactory in all domains of the assessed clinimetric properties, generic instruments (HAQ-DI, SF-36) had the more robust measurement properties. Correlations with clinical characteristics, other instruments and change in scores coupled with clinical change, strengthened their construct and concurrent validity as well as responsiveness. The SF-36 and HAQ-DI have been endorsed by the OMERACT group as validated tools to measure HRQOL and functional disability in gout (Singh, Taylor et al. 2011 and Schumacher, Taylor et al. 2009).

Since its development in the 1980s, the HAQ-DI has been used across disease entities as a predictor of healthcare utilisation, work disability, morbidity and mortality (Krishnan, Sokka et al. 2004). It has since been validated in clinical studies of chronic gout (Taylor, Colvine et al. 2008; Becker, Schumacher et al. 2009; Alvarez-Hernandez, Pelaez-Ballesteros et al. 2008; Ten Klooster, Oude Voshaar et al. 2011). Correlations between the HAQ-DI and gout characteristics, such as the number of attacks in the past 6 months, tender and swollen joints, were moderate (0.30 to 0.59) to high (> 0.60) but universally high for general measures such pain and number of sick leave days (Taylor, Colvine et al. 2008). The HAQ-DI also correlated well with patient as well as physician global assessment (0.77) which is not seen in the disease-specific GIS outlined below. The upper limb focus of the HAQ-DI (through domains such as dressing and grooming, grip, eating and reach) is also illustrated in its excellent correlation with measures of upper limb disability, such as the

Disability of the Arm, Shoulder and Hand (DASH) (Hudak, Amadio et al. 1996), Sollerman's test (Sollerman, Ejeskär 1995), HAQ II and lower correlations with the SF-36 social and emotional health and role limitation subscales (Taylor, Colvine et al. 2008; Alvarez-Hernandez, Pelaez-Ballestas et al. 2008 and Ten Klooster, Oude Voshaar et al. 2011). The HAQ-DI had poor correlation with the SF-36 MCS, which is in contrast to the GIS. This may indirectly highlight the differences in the approach to HRQOL by the HAQ-DI and the GIS. As opposed to physical functioning in the HAQ-DI, the GIS focuses on psycho-social well-being through assessment of the concern for gout in the acute as well as inter-critical phase, as well as the satisfaction with treatment. The HAQ-DI also had significant floor effect (20.5 % (Taylor, Colvine et al. 2008) and 42.2%(Alvarez-Hernandez, Pelaez-Ballestas et al. 2008)) indicating a lack of discriminatory ability amongst those with low levels of disability.

Although the HAQ II was developed to overcome the floor effects seen in the HAQ-DI, 25.8% of participants in a Dutch study were deemed to have no disability (Ten Klooster, Oude Voshaar et al. 2011). The HAQ II has very strong correlation (0.87) with the HAQ-DI and strong correlation with the PF-10 (-0.79) (Ten Klooster, Oude Voshaar et al. 2011). The PF-10 is a 10 - item scale of the SF-36 which measures limitations in physical activities (scores 0 – 100, higher indicating better health) (Haley, McHorney et al. 1994). Despite having negligible floor and ceiling effects, the discriminatory properties of the PF-10 based on self- reported general health were poor, with participants in the good health group scoring higher than those in the excellent group. Known group validity (based on joints with functional limitation) was also poor for the MOS 20 (Alvarez-Hernandez, Zamudio-Lerma et al. 2009), another variant of the SF-36. In keeping with SF-36, psychological HRQOL (mental health and health perception subscales) was no different between those with and without joints with functional limitation. Sensitivity to change after 8 weeks was limited to the physical and social function and health perception subscales. However, a time span

of 8 weeks in the context of a chronic relapsing remitting disease such as gout may not be long enough to demonstrate a significant change in mental well being.

In the SF-36, lower MCS scores (worse health) were seen in the presence of polyarticular disease whereas tophi, co-morbidities and radiographic damage in addition to the polyarticular joint involvement led to lower PCS scores (Khanna, Perez-Ruiz et al. 2011). Although the scores of the PCS improved after treatment with colchicine and ULT for 12 months, no significant change was seen in the MCS (Khanna, Perez-Ruiz et al. 2011). These findings may imply that gout is a chronic relapsing and remitting condition that has lesser impact on psychological well-being. However it is more plausible that the MCS is less sensitive to detecting the influence of gout and its treatment on HRQOL. Unpredictable attacks followed by inter-critical periods, side effects of treatment (for example, diarrhoea due to colchicine) and the stigma associated with gout (Lindsay, Gow et al. 2011) are some reasons why psychological well-being may be affected in gout. Generic health questionnaires lack the specificity to target such issues. Whilst the generic instruments allow comparison between the impact of different diseases, their treatments and cost-effectiveness analyses, they may lack the sensitivity to capture the true impact of gout especially in those with less severe disease (Mazur, Kupiainen et al. 2011).

The GAQ 1.0 consisting of 7 sub-scales was the first gout-specific questionnaire developed to reflect the patients' experience of gout and its treatment on HRQOL. Correlations between the GAQ 1.0 subscales and the PCS of the SF-36 were better than those with the MCS, except for treatment convenience (Colwell, Hunt et al. 2006). Those enrolled in a phase 2 clinical trial of febuxostat with serum uric acid > 8 mg/dL (Colwell, Hunt et al. 2006) are likely to have a more severe form of gout (that may be refractory to conventional ULT) compared to the majority of

people with gout treated in primary care. Hence these findings may not be generalizable to those presenting with gout in primary care, treated with traditional ULT.

The disease-specific GIS derived from modifications made to the GAQ 1.0 (Khanna, Sarkin et al. 2011; Hirsch, Lee et al. 2008) has better correlation with patient-reported factors (attack frequency over the last 12 months, patient rated severity, typical attack pain over the past 3 months) and may be more responsive to small changes in health status (Hirsch, Lee et al. 2008). The during attack subscales had better correlation with typical attack pain over the past 3 months, perhaps indicating better recall, when compared to attack frequency over the last 12 months, which may vary greatly between participants. The unmet treatment need subscale correlated with serum uric acid and physician-rated severity, both non-patient-reported factors which may be influenced by the success of treatment. In contrast to the GAQ 1.0, correlation of the GIS subscales with the MCS component of the SF-36v2 (-0.17 to -0.43) was higher than the PCS (-0.10 to -0.20) which may reflect the stronger ability of the GIS to detect the impact of gout on a more personal and psychological level in both the acute and chronic phases. There was no correlation between the GIS and speciality of the treating physicians (Hirsch, Lee et al. 2008), which may allow for it to be used widely even in non-specialist settings. Although the GIS is specific to gout, it does not allow comparison between disease states. As yet, the OMERACT group has not fully endorsed the Gout Assessment Questionnaire 2.0 and its GIS sub-scale as fully validated HRQOL measures in chronic gout (Singh, Taylor et al. 2011)

A consistent finding of all the instruments reviewed is that people with gout had lower physical HRQOL compared to the normative distribution (Singh, Strand 2008; Lee, Hirsch et al. 2009) as well as study controls (Roddy, Zhang et al. 2007c) even after adjusting for co-morbidities (Lee,

Hirsch et al. 2009; Hirsch, Terkeltaub et al. 2010; Hirsch, Lee et al. 2008). This may be due to the stronger emphasis on physical functioning as an indicator of HRQOL in the generic instruments. In gout treated with colchicine and ULT (Khanna, Perez-Ruiz et al. 2011) as well as 'treatment failure gout' (Becker, Schumacher et al. 2009) the SF-36 v 2 PCS score was lower than the MCS scores. Similarly scores of the HAQ-DI demonstrated physical limitations in gout, although the nature of the disability was milder in gout where treatment was not specified compared to treatment failure gout and other chronic rheumatic diseases such as RA or osteoarthritis. Gout concern overall, concern and well-being during attack remained above the midpoint of the scale (arbitrary cut-off described by Hirsch et al (Hirsch, Terkeltaub et al. 2010)) despite receiving treatment, which was generally perceived as satisfactory and not causing concerning side-effects. Further qualitative studies may elaborate on whether this is due to a lack of understanding of the role of ULT and low expectations from the treatment.

Co-morbidities (medical and musculoskeletal) and gout-related characteristics have both been associated with poor HRQOL. Physical HRQOL (SF-36 and HAQ-DI) was lower in the presence of co-morbidities. The high burden of co-morbid conditions in gout may be more easily detected through generic questionnaires due to the broader range of health enquiry incorporated in these. Subjective gout characteristics (frequency of attacks in the last 12 months, pain in between and during a typical attack) were most strongly associated with poor HRQOL in cross-sectional studies independent of co-morbidities in both gout-specific and generic questionnaires. Other gout characteristics associated with poor HRQOL were: uncertainty regarding the presence of tophi, pattern of joint involvement, time since last gout attack and physician-rated severity.

The impact of SUA and tophi were variable, with some studies reporting an adverse effect on HRQOL (Khanna, Perez-Ruiz et al. 2011; Hirsch, Terkeltaub et al. 2010) but others showing no effect (Roddy, Zhang et al. 2007c; Sarkin, Levack et al. 2010). SUA may have an indirect

relationship with HRQOL in gout, as it is positively correlated with the frequency of attacks in the last 12 months as well development of tophi (Alvarez-Nemegyei, Cen-Piste et al. 2005; Khanna, Nuki et al. 2012; Shoji, Yamanaka et al. 2004). Although allopurinol is not perceived by patients to improve HRQOL (Roddy, Zhang et al. 2007c; Alvarez-Nemegyei, Cen-Piste et al. 2005), use in primary care is often suboptimal (Roddy, Zhang et al. 2007b) and it has been shown to reduce the number of attacks as well as tophi (Perez-Ruiz, Lioté 2007; Briesacher, Andrade et al. 2008). Patients may be unaware of the rationale behind ULT, with many discontinuing treatment at the onset of attacks when ULT is initiated (Harrold, Mazon et al. 2010).

3.6.1 Strengths and limitations of this review

The strengths of this review are data extraction and quality assessment using validated tools by two independent reviewers. This search strategy included a filter which is 90-97% sensitive in retrieving clinimetric articles (Terwee, Bot et al. 2007) optimizing the power of the search to identify all relevant articles. Reference lists of retrieved articles were hand searched for additional articles that may have been missed in the electronic search. Despite this robust approach some articles may have been missed.

HRQOL is a subjective concept which is influenced by personal as well as cultural beliefs. Excluding non-English articles (French, Spanish, Russian and German) prevented comparisons across culturally heterogeneous study populations. Grey literature (conference abstracts) was excluded based on the lack of sufficient detail for inclusion into the review or later publication as a peer reviewed journal article. Some limitations could be attributed to the nature of the literature reviewed. The generalizability of the results may be limited by highly selective populations studied (treatment-failure or chronic tophaceous gout in the inter-critical stage, mainly Caucasian males), study settings (private or specialist clinics) and variable response rates. There is heterogeneity in the way studies reported their results, some presenting scores of

HRQOL whilst others specifying correlation coefficients between covariates and the outcome measure. Completion of self-reported questionnaires, physician assessment of severity and recording of markers of disease activity (SUA, tophi) may all have happened at different time points, which may weaken the association between these variables.

3.6.2 Implications of the findings of this review for future research

Existing studies of HRQOL in gout are limited by their paucity of longitudinal data, recruitment from highly selective secondary care populations and use of mostly generic instruments to measure HRQOL. Although validated to measure HRQOL in gout, generic instruments may focus on physical disability and miss patients' perception of the impact of gout and its treatment on other aspects of HRQOL. Hence there is a need for a primary care-based prospective cohort study using gout-specific and generic questionnaires to determine how HRQOL changes over time in the clinical setting where most patients with gout are treated i.e. primary care, identify which factors (such as disease characteristics, treatment, co-morbidities including anxiety and depression) predict change in HRQOL and also enable those at risk of deterioration to be identified and better-targeted for treatment.

3.7 Conclusion

This chapter provided a review of the existing literature on HRQOL in gout, including the measurement properties of the instruments used to measure HRQOL. The associates (gout and other characteristics) of HRQOL were identified and a narrative summary of the evidence for the associations was presented. The next chapter in the thesis describes the methods used to set up a cohort of participants with gout in primary care. It then focuses on how HRQOL was measured using a combination of generic and gout-specific questionnaires in the baseline phase of the

cohort study. From there on, the thesis is concerned with HRQOL in the baseline or cross-sectional phase only.

4 A cross-sectional study of Health Related Quality of Life (HRQOL) in gout: Design and Methods

4.1 Introduction

The previous chapter identified the existing studies on Health Related Quality of Life (HRQOL) and the questionnaires used to measure this concept in gout. Poor HRQOL was associated with gout as well as co-morbid characteristics. However majority of the studies identified were based in specialist settings and measured HRQOL by using generic questionnaires. The findings of the systematic review in the previous chapter have informed the design of this cross-sectional study of HRQOL in gout, which is nested within a primary care-based cohort study. This chapter presents the design of the study and the methods of all data collection procedures relevant to this thesis.

4.2 Design

This study is conducted within a primary care-based cohort with a total follow-up duration of 3 years. This thesis however is concerned with the cross-sectional phase of the study only, components of which have been shaded grey in the schematic flowchart of the wider study (see Figure 3)

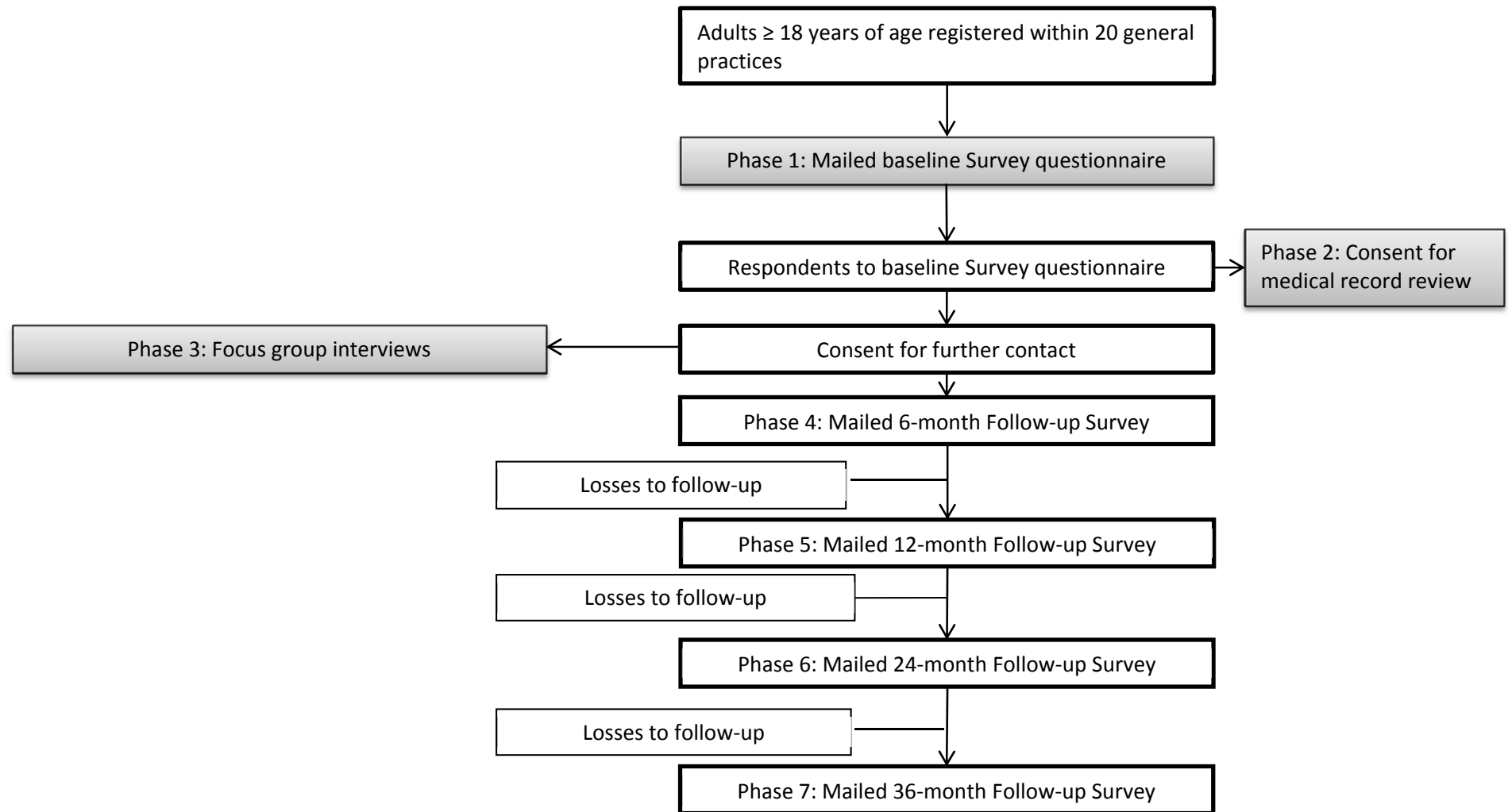


Figure 3: Flowchart of the cohort study phases

The target population for the cross-sectional study were community dwelling adults (aged ≥ 18 years) registered within 20 general practices in the West Midlands. This age cut-off point was selected as gout (primary or secondary, i.e. diuretic induced (Roddy, Doherty 2010)) is rare in those aged under 20 years, with a prevalence of 5.11 cases per 100,000 (Kuo, Grainge et al. 2014). Twenty general practices were used as they provided the adequate number of participants, as described in the sample size calculation in section 4.4. The remainder of this section elaborates on the eligibility criteria, recruitment process and contents of the baseline questionnaire. The majority of this information has been published previously as a peer-reviewed research protocol paper ((Chandratre, Mallen et al. 2012), Appendix 2)

4.2.1 Patient eligibility

4.2.1.1 Inclusion criteria

- a) Registered with the participating general practice during the study
- b) Read code consultation (Table 4-1) for gout or prescription for colchicine or allopurinol during the preceding two years
- c) Provided written informed consent for participation in the study

4.2.1.2 Exclusion criteria

- a) Under 18 years of age
- b) Vulnerable groups – e.g. significant cognitive impairment, severe enduring mental illness, active malignancy or other terminal illness.

4.2.2 Phase 1: Cross-sectional survey

4.2.2.1 Recruitment procedures

All potentially eligible patients registered within the participating general practices were identified through standard Read codes (Table 4-1) used for gout or prescription of colchicine or allopurinol. The following Read codes were used;

Table 4-1: Read Codes for identification of those with a diagnosis of gout in primary care

Code	Term
C34	Gout
N023	Gouty arthritis
EGTON 227	Gout NOS
OX2740G	Gout Acute /ox
1443	H/O: gout
EMISR4QG01	Gouty tophi + Gout NOS
2D52	O/E - auricle of ear - tophi
669	Gout monitoring

Staff from the West Midlands North Primary Care Research Network (WMN PCRN) conducted a one-off electronic search of the primary care records in participating practices to identify patients with a consultation for gout or a prescription for colchicine or allopurinol within the last two years. The names and contact details of the eligible patients were stored in a password-protected mailing database and held on the university's firewall and password-protected server. No other information from the patients' primary care records were accessed or stored unless and until informed written consent to do so was obtained from the patient. The WMN PCRN team members screened the mailing lists (prior to mailing) for patient deaths and departures from the practice to ensure that patients were not inappropriately contacted. The lead general

practitioner (GP) at each practice was invited to identify potentially vulnerable patients to be excluded.

All eligible patients were sent a study pack from their general practitioner (on general practice headed notepaper). This contained a letter of invitation (appendix 5), participant information sheet (PIS) (appendix 6), a pre-paid return envelope and a baseline self-administered questionnaire (appendix 3) which also included a consent form asking for consent:

- I. For further contact by post
- II. For review of their medical records

Potential participants were also provided with a contact name and telephone number should they have any queries about the study. Patients were informed that they are under no obligation to participate and that if they were to decline their normal clinical care would not be affected in any way. On return of the questionnaire the response was recorded against a unique patient number – this included completed questionnaires, contact details, request to be excluded from the study and non-responders. The self-reported date of birth (for each unique participant identification number) in the baseline questionnaire was checked against the date of birth in the list from the general practices to ensure that the intended person had completed the questionnaire. Where the date of birth did not match, names and addresses were used to judge whether the data in the completed questionnaire could be assumed to be from the intended person.

Intended participants returning their questionnaires with the consent sheet and those who wished to be excluded from the study (non-consenting responders) were logged on the database so that no further reminders were sent to them. The mailing database determined future mailings.

4.2.2.2 *Non-responders to mailed study pack*

As per the ARUKPCC questionnaire mailing Standard Operating Procedure, non-responders to the initial questionnaire were sent a reminder postcard two weeks later. Non-responders to the postcard were sent a further baseline questionnaire two weeks later (4 weeks after the first questionnaire) (Mallen, Peat et al. 2006). This approach maximises response without placing significant burden on patients. Those who failed to respond after all three baseline mailings were assumed not to have consented to the study and were not contacted again.

4.2.2.3 *Data management - entry, coding, cleaning and storage*

Data was entered into a study specific database (mailing, demographics and questionnaire data) by dedicated members of the administrative team as the completed questionnaires were returned. Although they were experienced in data entry, specific training was provided for this study. All data within the questionnaire were coded prior to data entry into the database. Some standard codes (e.g. missing data (-9), not applicable (-88)) are used by the research centre and were also utilised in this study. One in ten random questionnaires was checked by a member of the study team for the purposes of quality assurance. This information is kept by the study co-ordinator (Helen Myers) and study statistician (Sara Muller). Data was cleaned to ensure that participants' data were accurately entered into the study database. Only relevant members of the research team were granted access to the password-protected database. Questionnaires and consent sheets were securely stored in separate locations in the ARUKPCC, to protect the confidentiality of the patients.

4.2.2.4 *Questionnaire content*

The baseline questionnaire was divided into 7 main sections, each designed to capture gout-specific, co-morbid, lifestyle and socio-demographic characteristics of the survey responders.

- I. Gout symptoms and treatment
- II. The impact of gout on daily life (using the Gout Impact Scale)
- III. General health (including co-morbidities and measures of physical function)
- IV. Measures of anxiety and depression in gout patients
- V. Foot and other joint problems (data pertaining to this section has not been analysed for inclusion in this thesis hence this will not be discussed in further detail from here onwards)
- VI. Occupational characteristics
- VII. Socio-economic and demographic characteristics

Details of the conceptual domains, operational definitions and empirical measures are provided in Table 4-2. The sections below describe in detail, the collection and analyses of data from the wider study that has been used in this thesis.

Table 4-2: Self-complete postal questionnaires: conceptual domains, operational definitions and empirical measures

Conceptual domain	Operational definition	Empirical measure	Number of items
I. About gout			
Gout frequency	No. of attacks in the last 12 months/since last contact	Response options 0, 1, 2, 3, 4, ≥5	1
Age at diagnosis	Age in years	Numerical free text box	1
Acute attack of gout	Acute episode at time of questionnaire	Yes/ No	1
More than one joint involved in an acute attack of gout at any given time	Mono/oligo or polyarticular attacks of gout	Yes/No	1
Allopurinol	Reported use of allopurinol	Yes/No	1
	Current daily dose of allopurinol	Nine daily dose options: 50 mg-900 mg	1
II. How gout affects your life			
Gout concern, wellbeing, productivity, convenience and satisfaction	GIS (Hirsch, Lee et al. 2008)	5-item Likert scale	18
Illness perception	Modified IPQ (Moss-Morris, Weinman et al. 2002)	5-item Likert scale	4
III. General health			

Conceptual domain	Operational definition	Empirical measure	Number of items
Physical function	SF36 PF-10 (Ware, Sherbourne 1992)	3-item Likert scale	10
	HAQ-DI (Bruce, Fries 2003a)	4-item Likert scale	17
Co-morbidities	Diabetes mellitus, Renal failure, Renal calculi, stroke ,TIA, MI, angina, hyperlipidaemia and hypertension	Yes / No	9
IV. How you feel			
Anxiety and depression	PHQ 9 (Kroenke, Spitzer et al. 2001)	4-point Likert scale	16
	GAD- 7 (Spitzer, Kroenke et al. 2006)		
V. Foot and other joint problems			
Hallux valgus	Self-completed line drawings (Roddy, Zhang et al. 2007a)	5 line-drawings for each foot depicting increasing severity of hallux valgus	2
Pain	Pain in the hands, hips, knees and feet in the last year	Yes/No	4
	Location of body pain in last 4 weeks	Self-completed body manikin (Hunt, Silman et al. 1999) (Lacey, Lewis et al. 2005)	1
Foot pain	Foot pain, aching, stiffness in last month (Dufour, Broe et al. 2009)	Frequency on 5-point Likert scale	1

Conceptual domain	Operational definition	Empirical measure	Number of items
Foot pain location	Location of foot pain in last four weeks	Self-completed foot manikin (Garrow, Silman et al. 2004)	1
Foot function	MFPDI (Menz, Tiedemann et al. 2006)	Frequency on 3-point Likert scale	17
Consultation for foot problems	Consultation with GP, physiotherapy, podiatry, chiropody since last 12 months/since last contact	Yes/No	4
VI. Work			
Occupational characteristics	Current employment status	11-response options	1
	Work absence during last 6 months due to joint/back problems	Yes/No	1
	Ability to do usual job	5-response options	1
VII. Demographic / socio-economic characteristics			
Date of birth and gender	Date of birth and gender	Date of birth, male/female	2
Anthropometric characteristics	Height	Meters or feet/inches	1
	Weight	Kilogram or stones/pounds	1
Relationship status	Marital status	6-response options	1

Conceptual domain	Operational definition	Empirical measure	Number of items
Education	Higher education	Yes/No	1
Ethnicity	Ethnicity	6-response options	1
Life-style-characteristics	Frequency of alcohol consumption	6-response options	1
	Weekly amount of beer/spirits/wine consumed	Free-text	1

Abbreviations: GIS; Gout Impact Scale, HAQ-DI; Health Assessment Questionnaire Disability Index, SF 36 PF-10; Short Form 36 Physical Function-10 subscale, IPQ; Illness Perception Questionnaire, PHQ-9; Patient Health Questionnaire-9, GAD-7; Generalised Anxiety Disorder-7, MI; Myocardial Infarction, TIA; Transient Ischaemic Attack, MFPDI; Manchester Foot Pain Disability Index

4.2.3 Gout-specific characteristics

Survey participants were grouped by self-reported attack frequency over the last 12 months, pattern of joint involvement (history of gout attack in 1 (mono) versus 2 to 4 (oligo) or ≥ 5 joints (polyarticular (Schumacher Jr, Habre et al. 2004)), acute attack at the time of questionnaire completion as well as urate-lowering treatment with allopurinol (and the dose taken). The dose of allopurinol was reported as a pre-defined dose in 100 mg increments from 100 mg to 900 mg, and / or entered as a free-text numerical value (by those who were on an unconventional dose of allopurinol). Disease duration was calculated by subtracting the age at diagnosis of gout from the current age (calculated from the date of birth).

4.2.4 The impact of gout on quality of life

Although still in the early stages of its development, the Gout Impact Scale (GIS) has been shown to have good content validity with direct patient input (Hirsch, Lee et al. 2008), moderate correlation with patient rated disease severity and is responsive to change (Khanna, Sarkin et al. 2011). The gout-specific GIS comprising of 5 subscales (concern overall, medication side-effects, unmet treatment need, wellbeing and concern during attack) each rated on a 5-point Likert scale, was employed to assess the impact of gout on all aspects of HRQOL. The scores of the GIS were calculated in accordance with published scoring guidelines (Hirsch, Lee et al. 2008) and personal communication via electronic mail with Dr J Hirsch, by the study statistician (Dr Sara Muller). Scores for each sub-scale ranged from 0 to 100, higher scores indicating worse health or greater impact of gout (Hirsch, Lee et al. 2008). Scores of the GIS were treated as a continuous variable for analysis purposes.

Also included in the baseline questionnaire were 4 questions (each rated on a 5-point Likert scale ranging from strongly disagree to strongly agree) adapted from the revised illness perception

questionnaire (IPQ-R) (Moss-Morris, Weinman et al. 2002). These questions assess the perception of gout severity, treatment effectiveness and the effect of personal actions on the course of the disease. These data are not included in the results presented in this thesis.

4.2.5 General health and co-morbidities

Participants were asked to report any formal diagnoses of stroke, transient ischaemic attacks (TIA), hypertension, hyperlipidaemia, myocardial infarction, angina, diabetes, renal calculi and renal failure. Activity limitation during the preceding one week was assessed through the Health Assessment Questionnaire Disability Index (HAQ-DI), comprising of 8 categories (dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities) containing 20 items rated on a 4 point Likert scale (ranging from without any difficulty to unable to do) (Bruce, Fries 2003a). The use of aids or devices and help from others in order to complete a task have been incorporated in the HAQ-DI. Pain and global Visual Analogue Scales (VAS) (part of the HAQ-DI but scored separately) were also included in the baseline questionnaire. The clinimetric properties of the HAQ-DI have been described in detail in chapter 3 (systematic review). Based on its internal consistency (Taylor, Colvine et al. 2008), test-retest reliability (Alvarez-Hernandez, Pelaez-Ballestas et al. 2008) and correlation with clinical characteristics (general health, co-morbidities and gout characteristics) (Ten Klooster, Oude Voshaar et al. 2011) the Outcome Measures in Rheumatology Clinical Trials (OMERACT) group endorsed it as a validated tool to measure HRQOL in gout at their 10th annual meeting (Singh, Taylor et al. 2011). Another generic questionnaire approved by OMERACT in measuring HRQOL in gout is the Medical Outcomes Study Short Form 36 (SF-36) (Singh, Taylor et al. 2011). The Physical Function 10 (PF-10) subscale of the SF-36 was used in the baseline questionnaire to measure limitations in physical activity, mobility and activities of daily living (ADL) during the preceding 4 weeks (White, Wilson et al. 2011). The lower ability of the PF-10 in discriminating between different levels of general health compared to

the HAQ-DI may be attributed to unequal number of participants within each level or collapsing the excellent and very good health into one level. PF-10 however has lower ceiling effects compared to HAQ-DI meaning a lower number of participants had the best possible physical function score. It also had good internal consistency (0.94) and correlation with the HAQ-DI (Ten Klooster, Oude Voshaar et al. 2011). As the PF-10 is shorter than the Medical Outcomes Survey Short Form 36 (SF-36) in its entirety, it has low respondent burden (10 minutes to complete and questions worded at sixth to ninth grade level (White, Wilson et al. 2011)). It was hoped that the combined use of the HAQ-DI and PF-10 would result in optimal clinimetric quality as well as the lowest possible respondent burden. The HAQ-DI and PF-10 were scored by the study statistician (Dr Sara Muller) in accordance with published guidelines (Bruce, Fries 2003a) (Ware, Kosinski et al. 2000). Higher scores (range 0 to 3) on the HAQ-DI indicate worse activity limitation. Lower scores for the PF 10 (range 0 to 100) indicate greater functional limitations.

4.2.6 Anxiety and depression

The Generalised Anxiety Disorder (GAD) self-report questionnaire consists of 7 items which aim to measure the frequency of anxiety and related thoughts (ranging from not at all to nearly every day) during a preceding 2-week period. Each of the 7 items can be scored from 0 to 4, therefore the over-all score of the GAD-7 ranges from 0 to 21 (higher scores indicating increasing severity) (Spitzer, Kroenke et al. 2006). Cut-off points for mild, moderate and severe anxiety have been suggested as 5, 10 and 15 respectively (Spitzer, Kroenke et al. 2006).

Although independent disease entities, anxiety and depression do correlate highly with each other (Bjelland, Dahl et al. 2002). Hence the impact of depression (co-existing with gout) on HRQOL was assessed using the Patient Health Questionnaire (PHQ)-9, containing the 9 items that aid diagnosis of depression in the Diagnostic and Statistical Manual of Mental Disorders fourth

edition (DSM- IV) (Kroenke, Spitzer 2002). Similar to the GAD-7, each of the 9 items refer to feelings during the preceding 2 weeks and can be scored from 0 (not at all) to 3 (nearly every day). Scores of 5 to 9 indicate mild, 10 to 14 moderate, 15 to 19 moderately severe and 20 to 27 severe depression (Kroenke, Spitzer et al. 2001). Survey responders were categorised into anxiety and depression severity groups according to their scores. Both questionnaires were scored by the study statistician (Dr Sara Muller).

4.2.7 Generalised body pain

Pain in the preceding one month affecting any part of the body and lasting for one day or longer was ascertained by a single question with a dichotomous (yes/no) response option (Lacey, Lewis et al. 2005). The data pertaining to the precise locations of pain in the manikin have not been used in this thesis.

4.2.8 Socio-demographic and lifestyle characteristics

Neighbourhood deprivation quintiles were based on ranks of indices of multiple deprivation (Department for Communities and Local Government 2007), calculated using the participant's post-code. Self-reported height and weight were used to calculate Body Mass index (BMI) which was categorised into underweight, normal, overweight and obese according to the World Health Organisation classification criteria (WHO Expert Consultation 2004). Survey responders were dichotomised according to relationship status (living alone/ married or cohabiting), ethnicity (Caucasian/ non-Caucasian), attendance at a higher education institution (yes/ no) and age at leaving higher education (under/ over 21 years). Frequency of alcohol intake was categorised from 'never' to 'daily' in six response options.

4.3 Phase 2: Review of general practice medical records

All participants in Phase 1 who gave permission for their GP records to be accessed had their computerised medical records tagged by a member of the WMN PCRN team. All relevant gout-related consultations or prescription for colchicine or allopurinol in the 2 years preceding the study were identified using search techniques based on Read codes and free-text entries. Such searches have already been developed and successfully applied for foot and knee-related consultations in the Centre's cohorts (Bedson, Mottram et al. 2007) (Blagojevic, Jinks et al. 2008). The practices participating in this study are fully computerised and undergo annual audits completed by the Primary Care Research Network to assess the quality and completeness of the data entry at the practices (Porcheret, Hughes et al. 2004). Serum Uric Acid (SUA) and tophi were ascertained from free text entries in the medical records of consenting participants. The data were exported into a password-protected file and then stored on an encrypted data storage device (complaint with NHS guidelines for data encryption) or emailed using the NHS approved electronic mail service NHS.net. All sensitive data (name, contact details) were removed from the medical records and the consultation data were linked to the survey data by unique survey identifier.

4.4 Sample size

As the sample size for the overall cohort pertained to change in HRQOL over the duration of 3 years, a formal sample size calculation specific to the cross-sectional phase of the study was not performed. In order to use the information recorded at all five time-points, a sample size of 882 would allow a smallest meaningful difference in HRQOL of 0.2 standard deviation units to be detected between two groups (441 subjects per group) defined in terms of frequency of gout attacks (<2 attacks, ≥ 2 attacks per year) using a linear mixed model (significance 0.05, power 90%, autocorrelation 0.8) (Diggle 2002). Allowing for 70% response at baseline and 30% drop out over

the follow-up period would require 1800 people with gout to be contacted at baseline. These calculations were provided by the study Principal Investigator (Dr E Roddy).

4.5 Statistical analysis

Cleaned data was transferred from the study database to SPSS (version 20, SPSS Inc., Chicago, IL) for analysis purposes.

4.5.1 Creating new variables in SPSS

Where possible and appropriate, independent continuous variables were recoded into more manageable categorical variables – for example, age, disease duration, frequency of attacks, allopurinol dose, age at leaving further education, anxiety, depression, multiple index of deprivation ranks, alcohol frequency, serum uric acid and BMI. Other independent variables had binary outcomes – gender, currently having an attack of gout, oligo or polyarticular attacks, presence of tophi, current use of allopurinol, presence of co-morbidities, generalised body pain, relationship status (married or co-habiting and others) and ethnicity (Caucasian and others). Dependent continuous variables (scores of HRQOL - GIS, HAQ-DI, PF- 10) were left unchanged.

4.5.2 Flow of participants through the cross-sectional study and HRQOL scores grouped by participant characteristics

Data from the self-completed questionnaire and general practice medical records were analysed as follows:

- Descriptive account (frequency and percentages) of flow of participants: eligible, mailed, responded, consented and followed up

- Age, gender and neighbourhood deprivation scores were compared between baseline responders and non-responders.
- Simple descriptive statistics (frequency and mean (standard deviation) or median (interquartile range) described the baseline characteristics of the study population, for example demographics, anthropometrics, gout duration, gout attack frequency, history of oligo or polyarticular attacks, use of allopurinol, currently having an attack of gout, psycho-social factors, co-morbidities and musculoskeletal pain
- The scores of HRQOL (overall mean and standard deviation) were calculated for the study population and then compared between sub-groups defined according to socio-demographic, co-morbid and gout-specific characteristics. Differences between mean scores of HRQOL were tested using independent samples t-test (variables with binary outcomes) and one- way Analysis of Variance (variables with categorical outcomes).

Full details of specific analyses performed are included in chapters pertaining to study response and HRQOL scores grouped by participant characteristics.

4.5.3 Association of HRQOL with independent variables

Univariate unadjusted β coefficients (95% confidence intervals) between HRQOL and independent variables such as gout characteristics (frequency of gout attacks, disease duration, use of allopurinol, currently having an attack of gout, oligo or polyarticular attacks), co-morbidities (hypertension, hyperlipidaemia, diabetes mellitus, renal disease, vascular disease, musculoskeletal pain), socio-demographic factors (age, gender, BMI, neighbourhood deprivation, alcohol intake, education) and psycho-social factors (anxiety, depression) were calculated. All variables were then entered into a multiple linear regression model (adjusted for other gout as well as non-gout characteristics) with HRQOL as the dependent variable. Details of specific analyses are provided in chapters 6 and 7.

4.5.4 Missing data

No substitutions were made for missing data (continuous or categorical). In the case of consent forms without a signature, any available data from the baseline questionnaires were retained for the study (to avoid the wasteful exclusion of completed questionnaires and prevent any adverse effects on data quality) but participants were excluded from follow-up phases of the cohort.

Although considered, multiple imputations for missing values were not performed after consultation with the study statistician (Milisa Bucknall). This was based on lack of change in β coefficient (and only a small change in standard error) when multiple imputations were performed for regression model (adjusted for other gout and socio-demographic characteristics) of oligo or polyarticular attack and GIS concern overall, selected at random.

4.6 Phase 3: Nested qualitative study

The purpose of this nested qualitative study was to explore patients' perspectives on how gout and its treatments affect HRQOL, using focus group interviews. The aim was to understand what aspects of gout and its treatments patients consider important and what impact these have on their day-to-day life.

4.6.1 Definition of focus group

The term focus group has historically been used interchangeably with 'group interviews' or 'focus group discussion' (Barbour 2008). The use of focus groups in the development of survey instruments dates back to the 1920s (Frey, Fontana 1991). A few decades later (1940-1950s) they were used to develop training and information materials and radio audience research (Merton, Kendall 1946). Focus groups rely on the interaction between group participants to generate novel ideas and promote discussion around the emerging topics (Barbour 2008). Although the focus of the interview is the interaction between participants, the interviewer or moderator plays an

important part in steering the direction of the discussion through a pre-determined (but not prescriptive) topic guide, bearing in mind the different personalities of the group members and aiding group interaction by exploring the different views expressed by the participants (Kitzinger 1995).

4.6.2 Focus group design

4.6.2.1 Filter questions from the baseline questionnaire

At the outset of the study design, a purposive sampling strategy was planned to ensure a wide mix of participants in the study. I discussed the sampling criteria with my supervisors (E Roddy, C Mallen and J Richardson) who had clinical and methodological expertise of gout and qualitative interviews. The key filter questions in the baseline questionnaire were:

- How many attacks of gout have you had in the last 12 months?
- Are you on a tablet called allopurinol for your gout?

The aim was to select participants with a wide range of gout attack frequency, ranging from 1 to ≥ 5 in a 12-month period, as well as a combination of those who were, and were not, on long-term ULT with allopurinol. By including such a mix of participants it was hoped that a wide range of issues which the patients consider important in the treatment of gout would be covered.

4.6.2.2 Gender of the interview participants

Although the severity of gout in women may be greater than men (Dirken-Heukensfeldt, Teunissen et al. 2010), it remains under-researched and under-reported in women. Gender homogeneity through over-sampling of women to develop an exclusively female group was

considered to facilitate interaction, help spontaneity and reduce any feelings of stigma or inhibition that may arise in a mixed group. The themes arising from an all-female group (as opposed to an all-male or mixed gender group) may highlight different perspectives on the impact of the treatment of gout on HRQOL (Lindsay, Gow et al. 2011). However practical issues such as availability to attend the interview and low response rate to interview invitation from women had to be considered alongside the pre-determined eligibility criteria for the groups. To get an in-depth insight into their experiences and facilitate equal participation, the size of the groups were limited to 5, in keeping with best practice recommendations (Kitzinger 1995).

4.6.2.3 Focus group interview locations

Three interviews were conducted at the Institute of Primary Care Sciences, Keele University and one in general practice after considering the geographic location of participants and willingness to travel to Keele University.

4.6.2.4 Participant selection and invitation

Participants for the focus group interviews were recruited from 603 participants who consented to further contact for research and completed the two filter questions in the baseline questionnaire. A total of 120 participants spread across a range of frequency of attacks in the preceding 12 months and treatment with allopurinol were then sent an invitation to the focus group interviews (appendix 7) by the administration staff. Non-responders were sent a reminder invitation letter (appendix 8) two weeks after the initial mail out. Those who did not reply to the reminder letter were deemed non-responders and were not contacted again. Forty-two potential participants who provided written consent to taking part in the interviews by returning the reply slip were then telephoned by the researcher to arrange an interview. Nineteen of these 42 were able to attend one of the four allocated interview dates. Written confirmation of the appointment was posted to the participants. As per the Standard Operating Procedure (SOP) of

the Institute of Primary Care Sciences, participants were reimbursed a flat fee of £15⁴ for their travel or offered a pre-paid taxi should they have required one. Drawing on expertise in qualitative interviewing within the study team, it was estimated that theoretical saturation (Kitzinger 1995) would be reached with approximately 20 participants.

Although the aim was to interview 20 participants in groups of 5, the total number of interviewees was 18 (including one carer) due to unforeseen bereavement and illness. Of the two female participants, one was not affected by gout herself but attended as a carer for her husband, who was one of the other participants. Other participants in the group provided consent to her presence and participation prior to the interview. After discussion with other members of the qualitative research team, it was felt that the views of a carer may add to the dimensions of the impact of gout and its treatments on HRQOL. The recruitment process for focus group interviews is summarised in Figure 4.

⁴ Personal communication with Rebecca Parker and Tracy Reynolds, finance and administration staff at the ARUKPCC

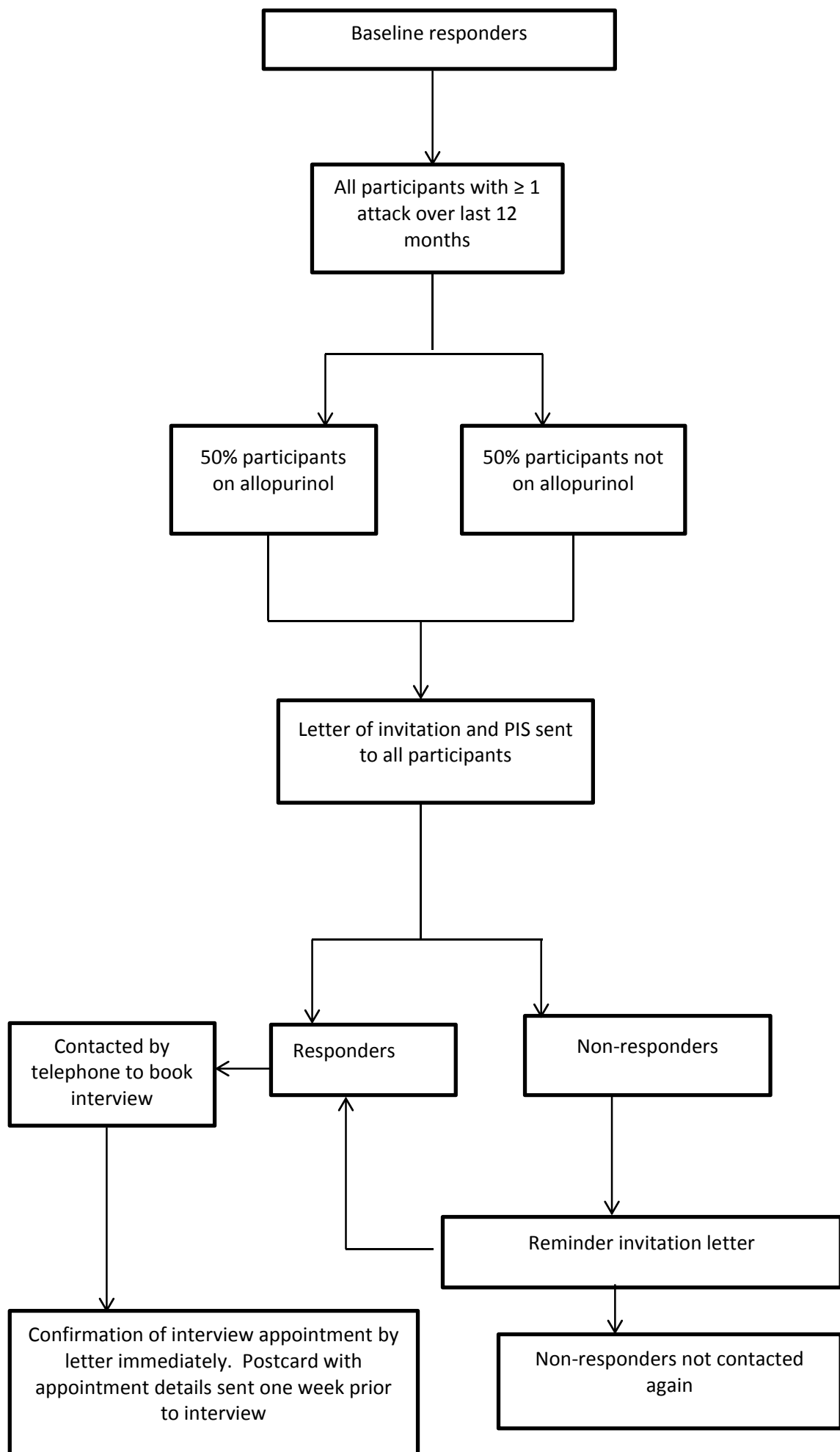


Figure 4: Recruitment process for the qualitative focus group interviews

4.6.2.5 Interview guide

The main question of focus group enquiry was:

“What impact has gout and its treatment had on your Quality of Life?”

The purpose of the topic guide was not intended to be prescriptive and participants were encouraged to lead the discussion. The interview guide was developed in conjunction with 5 lay persons or expert patients who have been diagnosed with gout who constitute the Gout Research Users Group (RUG). The key question regarding the impact of treatment of gout HRQOL was presented to the RUG to assess its relevance and generate associated questions which may be used as prompts by the moderator should the need arise. During the discussion with the RUG members I also identified some other key areas of interest not directly related to the interview question (for example, the role of diet).

4.6.2.6 Practical issues in arranging the interviews

Staggering the timing of the four interviews allowed reflection on those conducted previously and insight from these was used to inform the subsequent interviews. It also helped to avoid interviewer fatigue. All but one interviews were conducted at the ARUKPCC due to lack of sufficient numbers of participants at any one practice. A seating plan is included in appendix 9. As the moderator, I positioned myself so that I could monitor the engagement of all participants and prompt participation through visual as well as voice contact. As the single-handed organizer of the focus group interviews, I made a checklist to ensure that the interviews ran smoothly. The following aspects had to be planned in advance:

1. Timing of the interviews: Each of the initial 20 participants was telephoned and offered several time slots. Each time slot was blocked off once 5 participants were recruited to it. For

practical reasons (availability of rooms, refreshments, parking spaces, audio recorder, assistants, interviewer fatigue) I along with the study team decided to hold no more than one interview in a day.

2. Venue: For interviews held at the ARUKPCC, a standard room with a round table large enough to accommodate participants, moderator and assistant was booked. For one interview held at the GP surgery, I liaised with the practice manager to book a meeting room. Parking was reserved for all those participants who needed one by liaising with the administration staff at ARUKPCC.
3. Hosting the group: I liaised with the catering staff at the ARUKPCC to provide refreshments to the participants at ARUKPCC. I purchased refreshments for the participants invited to the GP surgery. Re-imbursement (cash for travel) were collected prior to the interview from the administration staff at ARUKPCC by myself and handed out to the participants at the end of the interviews by the assistant.

Assistants: I recruited three voluntary assistants (one assistant was present for two interviews) from within the staff and student members of the ARUKPCC.

4. Recording and transcription: Two digital audio-recorders were taken on loan from the ARUKPCC. All audio-recordings were uploaded to the project file on a password-protected drive on the ARUKPCC computer. These recordings were sent electronically to an external agency contracted by the ARUKPCC.

4.6.2.7 *The interview process*

Prior to the commencement of the group interviews, participants were provided with the opportunity to discuss any issues arising from the Patient Information Sheet (appendix 10). The rationale and procedure of the interviews including anonymised verbatim transcription of the audio recordings (by a university approved external agency) were made explicit to the

participants. Prior to the interview, participants were asked for informed written consent. The consent form was signed by the researcher and participants prior to the interview. Upon interview completion, the yellow carbon copy of the consent form signed at the start of the interview was returned to a member of the ARUKPCC administration team along with the list of interviewees. The member of the administration team could then log their participation in the interview on the study database.

Along with the interview assistants (Megan Bevis, Toby Helliwell and Carol Rhodes), I (interview moderator) was introduced to the participants as a researcher rather than a medical practitioner to ensure neutrality and maintain focus on patient perspective during the interviews. The interview assistants were responsible for taking notes during the interview and hospitality towards the participants. All participants were asked about the direct use of their quotations before (written consent form) and after the interviews (verbally) and all maintained their consent to the use of quotations at the end of the interviews. Although the participants' GPs were aware that they had taken part in the wider cross-sectional study, GPs were not specifically aware of participants' involvement in the interviews. This was to ensure that the participants could freely express their views without the fear of their GP (or other healthcare providers) becoming aware of their responses.

I summarized responses from the participants at regular intervals to demonstrate listening and understanding. Empathy and interest were also demonstrated through a number of verbal (affirmation) and non-verbal (nodding, eye contact, positive body language) communication strategies. The five stages of the focus group interviews are summarized below in Figure 5 (adapted from Ritchie, Lewis 2003).

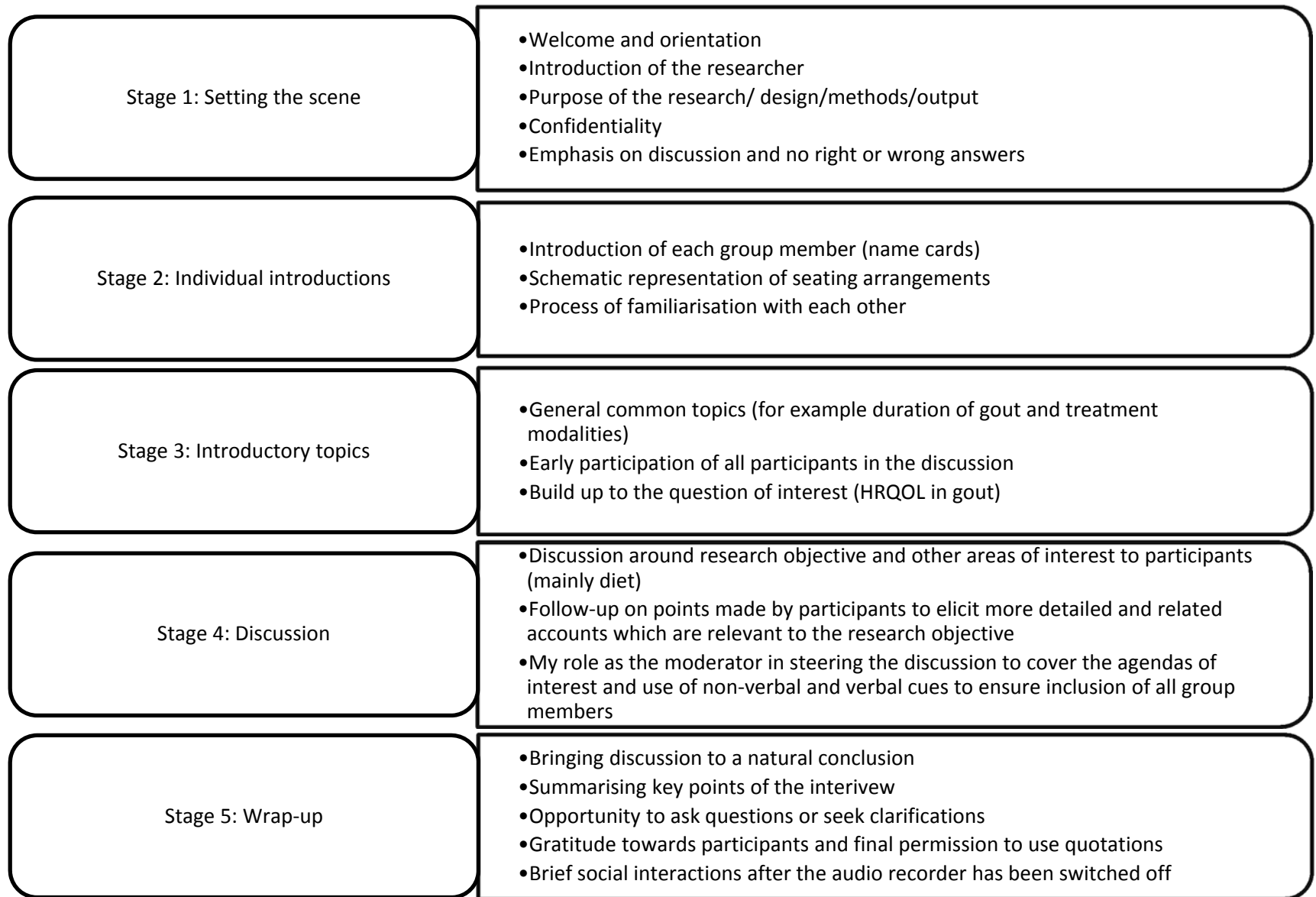


Figure 5: the 5 stages of a focus group interview

4.6.3 Data analysis

Data analysis within the thematic framework is traditionally done in 6 stages but is extremely flexible in how it is applied (Braun, Clarke 2006). As there are different manifestations of the methods, to suit the research question and data, flexibility was applied (Patton 1990) and stages 4 and 5 (reviewing and defining themes) were combined into the following 5 stages:

- I. Familiarisation with the data set
- II. Generating and clustering codes together
- III. Identification of themes
- IV. Review and definition of themes
- V. Production of the report

In this thesis, thematic analysis is used both within the realist framework which prioritises personal experiences and the constructionist framework that acknowledges that experiences and events are affected by a range of discourses within the society (Braun, Clarke 2006). The section below specifically describes how the 4 transcripts (generated from verbatim transcription of the 4 focus group interviews) fit into the above framework.

I scrutinised the original transcripts (formatted as word documents) and highlighted phrases relevant to the impact of gout (and its treatments) on all aspects of quality of life within the body of the text. Subsequently the highlighted phrases were examined again for key messages or explanations that were then written in the right hand column as 'codes'. In the third stage, codes used to annotate the main text that were similar in nature were clustered together. The clusters of codes were designated a theme in the left hand column. These themes were examined again in the final stage so that similar themes could be collapsed into one overarching theme or higher order descriptive label. Thematic analysis was data driven (inductive) as far as possible, however, as acknowledged earlier, my previous clinical experience may inevitably have contributed to some

degree of deductive analysis. The conceptual overview resulting from the 4 stage analytic process is represented in appendix 11. Higher order themes are displayed next to the themes and supported by the relevant extract from the text of the transcripts. The codes pertaining to the key words or phrases in the extracts are noted in the next column. Finally the number of the transcript along with the line number are presented within the table to enable referencing to the four transcripts (appendix 12) for purposes of transparency. Data analysis and interpretation were iterative as new themes emerged on repeated readings of the transcripts, until no new themes could be identified (theoretical saturation (Lindsay, Gow et al. 2011)). In order to ensure the robustness of the data analysis process, two independent reviewers with experience in qualitative research (Jane Richardson, PhD supervisor and Jennifer Liddle, an experienced qualitative researcher who has recently carried out in-depth interviews with people with gout) read and identified codes in two transcripts each. The narrative account of the participants' personal experiences was constructed after ensuring that the codes identified by the three reviewers were similar in nature. Codes identified by the three researchers were largely similar and as close to the text as possible. Any differences in the codes identified were discussed amongst the three researchers until a consensus was reached. I, as the researcher was solely responsible for interpretation of all the identified codes. In order to demonstrate transparency between the raw data and my interpretation of it, example quotations have been inserted throughout the narrative account.

4.6.3.1 Rationale for choosing thematic analysis method

It was intended that by virtue of its exploratory nature, the focus group interviews would give rise to previously unobserved data regarding the impact of gout and its treatment on HRQOL. Thematic analysis allows flexibility in the approach to data analysis with multi-directional

navigation through the entire dataset. An adapted form of Braun and Clarke's (Braun, Clarke 2006) six-phase approach to conducting thematic analysis was followed. This is described below.

4.6.3.2 *Thematic analysis*

Phase 1: Familiarisation with the dataset

Familiarisation with the transcripts is the basis of 'conceptual scaffolding' (Ritchie, Lewis 2003) which underpins the thematic framework. The audio recordings were transcribed verbatim by a university approved external transcription agency⁵ and served as raw data to be analysed. I read the interview transcripts on multiple occasions and compared these against audio recordings before identifying codes, sub-themes and themes. Data analysis was inductive – themes were data driven (derived directly from the transcripts) (Braun, Clarke 2006) and provide an insight into the experience of gout and its treatment unique to this set of participants.

Phase 2: Generating codes and clustering them together

The first step in the formation of the conceptual framework was to identify key descriptive terms (usually sentences or paragraphs) in the transcripts. By using sentences rather than single words, the context of the descriptive terms or codes were preserved. Codes similar in nature were clustered together. Coding was carried out manually for all four transcripts.

Phase 3: Identifying themes

Codes pertaining to similar topics or issues were grouped together into themes. Themes were both data driven and theory laden (concepts identified from previous literature review and clinical experience of managing patients with gout) (Braun, Clarke 2006). Themes similar in nature were then grouped under broader overarching themes or 'higher order categories' (Ritchie, Lewis

⁵ The Transcription Company UK (www.thetranscription.co.uk)

2003). Transcripts of each focus group were analysed until no new themes emerged (data saturation) (Braun, Clarke 2006).

Phase 4: Reviewing and defining themes

Themes that were similar in nature (coded data representing similar characteristics) were collapsed to form one unifying theme. Themes too broad (codes representing several different theories within a theme) were split further. Further review of the themes was carried out to assess the internal consistency of the coded extracts. Theories emerging from the themes were reviewed in the context of the overall meaning of the data set.

4.7 Peer review of the research protocol

The protocol for the conduct of the cohort study was submitted for an internal peer review process, at Keele University on 20th December 2011 (application for peer review included in appendix 13). As such a protocol for the conduct of the cross-sectional phase of the cohort study was not drafted separately. To enhance the scientific rigour of the qualitative methodology, the independent peer review committee suggested one-to-one interviews, greater emphasis on patients' perspectives in the interview guide and review of the interview data by more than one researcher. Although the interview guide was made less prescriptive and two additional reviewers were recruited to analyse the interview data, conducting several one-to-one interviews was considered outside the scope of this PhD thesis. The revised protocol (appendix 14) was awarded an outcome 1 (approval for submission to a local Research Ethics Committee) by the independent peer review committee on 24th February 2012. The approval letter (outcome 1) from the peer review committee along with their initial recommendations (outcome 2) are included in appendix 15.

4.8 Ethical approval

Ethical approval was sought from the North West Liverpool East Local Research Ethics Committee (REC reference number: 12/NW/0297, appendix 16) for all phases of the study, including the nested qualitative focus group interviews as well as the 6, 12, 24 and 36 months follow-up stages on 5th April 2012. The initial approval received on 30th April 2012 was conditional, pending revisions of the study protocol and accompanying study documents to include:

- Clarifications regarding the duration of data storage,
- Permission to regulatory authorities and NHS trusts to access data and medical notes
- Interview location
- Names and contact details of persons to contact should participants become distressed as a consequence of completing the questionnaire
- The option to leave the interview should a participant become distressed.

Names and contact numbers of NHS mental health support groups (Staffordshire brighter futures, mental health helpline Shropshire and Wolverhampton) were provided in the 'gout study participant information sheet version 2.0, dated 08/05/12' (appendix 6) as well as at the end of the questionnaire (baseline and all other follow-up time points, appendix 3). Specific interview location (ARUKPCC or GP surgery) and the option of leaving the interview if distressed in any way were also made explicit in the 'gout study participant information sheet for gout interview version 2.0, dated 08/05/12' (appendix 10). The consent form (part of the baseline questionnaire, appendix 3) included optional permission to allow individuals from regulatory authorities or NHS trusts to access medical records and self-reported data. Although the REC suggested destruction of the study questionnaires and interview data at the end of the study period, the proposal to store the data for 20 years to allow review, re-appraisal and re-checking, was in line with the Medical Research Council (MRC) recommendation (Strobl, Cave et al. 2000). The document

containing the suggested changes (along with their corresponding locations in the study documents) is included in appendix 17.

An amendment (personal communication via electronic mail) was proposed to the REC on 31st July 2012, to incorporate telephone contact with participants to arrange appointment times and places for the focus group interviews. This however was not considered to be a substantial amendment.

4.9 NHS Research and Development (R&D) approval

Approval to conduct the research at Staffordshire cluster of PCTs (which includes north and south Staffordshire, Stoke on Trent), Telford and Wrekin, Shropshire and Wolverhampton were gained in August 2012.

4.10 Personal contribution in the context of the wider study team

As the doctoral researcher and the study coordinator I drafted all study documents (relevant to the baseline and follow-up stages), including the patient information sheets (on GP headed paper), covering letters and study questionnaire. I coded the study questionnaire along with the study statistician (Sara Muller). The study specific database brief was drafted in collaboration with study statistician, Sara Muller and the database designer (Ms Zoe Mayson). I also drafted the applications for approval to conduct the research from the research ethics committee and site specific National Health Service (NHS) organisations using a single portal (Integrated Research Application System, IRAS). I attended the REC meeting at Alder Hay hospital, Liverpool, along with Dr E Roddy on 19th April 2012. Subsequently I drafted and re-submitted the study documents incorporating all amendments requested at this meeting. I performed all statistical analyses

(descriptive and regression) using SPSS version 21 and these were later verified by the study statistician (Milisa Bucknall).

4.11 Conclusion

The cross-sectional study of HRQOL in gout is nested within a three-year prospective cohort study. The cross-sectional study uses mixed methodologies (quantitative analysis of the self-complete questionnaires and qualitative analysis of focus group interview data). This chapter has outlined the study design, methods and analysis plans relevant to the focus of the PhD (cross-sectional only). The next chapter presents the analysis of the study response and differences in the socio-demographic characteristics of the responders and non-responders.

5 Cross-sectional survey of Health Related quality of Life in gout: Response and responder characteristics

5.1 Introduction

The previous chapter described the methods used to identify and recruit potential participants in a primary care-based cross-sectional survey of Health Related Quality of Life (HRQOL) in gout.

The methods of initiating contact with the participants, the mailing process and the contents of the questionnaire were also described in the previous chapter. This chapter aims to present the response to the survey (numbers mailed, excluded, responded, withdrawn and non-responders).

It then compares the socio-demographic characteristics of those who did and did not respond.

Lastly gout, co-morbid and socio-demographic characteristics of survey responders are described.

5.2 Aims

The aims of this chapter are to describe the flow of participants in the cross-sectional study.

Secondly response bias will be assessed through comparison of the socio-demographic differences between survey responders and non-responders. In addition, this chapter describes the gout-related and co-morbid characteristics of survey responders.

5.3 Objectives

The objectives relevant to the first aim are to provide a flow of participants through the cross-sectional study (those identified from primary care records, mailed after application of exclusion criteria, responding and non-responding and consenting to further contact and medical record review). In order to examine response bias (second aim), comparisons between the age, gender and neighbourhood deprivation indices of responders and non-responders will be presented.

Lastly, the gout-specific and co-morbid characteristics of responders will also be described.

5.4 Methods:

5.4.1 Study population

Potential participants aged ≥ 18 years who had a Read coded diagnosis of gout or were prescribed colchicine or allopurinol in the preceding two years, were identified from 20 General Practices within the West Midlands (West and North clusters). Prior to mailing, the potential participants were screened for relevant exclusion criteria (as described in chapter 3), death and departure from the general practice. Those eligible were sent a postal questionnaire. Those who returned the completed questionnaire were considered to be responders. In addition to completing the questionnaire, participants were also asked for consent for medical record review. Those who contacted the study team to be exempted from the survey (with or without reasons) were considered to have withdrawn from the study. Those who did not return the questionnaire after the reminder letter and repeat questionnaire (4 weeks after the initial mail-out) were considered as non-responders.

5.4.2 Questionnaire Content

Eligible participants were mailed a questionnaire containing self-reported gout, co-morbid and socio-demographic characteristics. Questions specific to gout included whether currently experiencing an attack, frequency of attacks in the preceding 12 months, history of oligo or polyarticular attacks and treatment with and dose of allopurinol. Disease duration was calculated by subtracting the age at diagnosis from the current age. Self-reported co-morbid conditions comprised diabetes, hypertension, hyperlipidaemia, stroke, transient ischaemic attack (TIA), renal calculi and failure, myocardial infarction (MI) and angina. The presence of any body pain was assessed using a filter question: "In the past 4 weeks, have you had pain that has lasted for one day or longer in any part of your body?" (Lacey, Lewis et al. 2005). Validated questionnaires, the Generalised Anxiety Disorder (GAD-7) and Patient Health Questionnaire (PHQ-9) were used to

assess anxiety and depression respectively. For the GAD-7, minimal anxiety was indicated by scores between 0 to 4, mild 5 to 9, moderate 10 to 14 and severe 15 to 21 (Spitzer, Kroenke et al. 2006). For the PHQ-9, minimal depression was indicated by a score of 0 to 4, mild 5 to 9, moderate 10 to 14, moderately-severe 15 to 19 and severe 20 to 27 (Kroenke, Spitzer et al. 2001). Socio-demographic characteristics comprised self-reported height, weight, frequency of alcohol intake, ethnicity, relationship status and level of education. Body Mass Index (BMI) was calculated from self-reported height and weight. Alcohol consumption was assessed through 6 response options ranging from never to daily intake. Ethnicity was dichotomised into Caucasian and non-Caucasian (Afro-Caribbean, Chinese, Asian, African and others) as the frequency of individual non-Caucasian ethnic groups was low (Asian 1.4%, Afro-Caribbean and African 0.2% each, Chinese 0.1% and others 0.6%). Relationship status was dichotomised into married/co-habiting and other (separated, divorced, widowed and single). Attendance at further education institution was dichotomised into yes and no. Those who reported attending further education were asked to report the age at which they left such further education. Age, gender and Multiple Deprivation Indices (MDI) ranks based on area post codes were available from the general practice records. The MDI rankings were split into quintiles (most deprived, second most deprived, mid deprived, second least deprived and least deprived). HRQOL was assessed through the generic Physical Function (PF-10) questionnaire comprising of 10 items and Health Assessment Questionnaire Disability Index (HAQ-DI) comprising of 8 categories including the use of aids/devices and help from another person and a gout-specific questionnaire, the Gout Impact Scale (GIS) comprising of 5 sub-scales assessing concern overall (CO), medication side-effects (MSE), unmet treatment need (UTN), well-being during attack (WBDA) and concern during an attack (CDA).

5.4.3 Medical record review

Tophi and Serum Uric Acid (SUA) were ascertained from medical record review for two years preceding the study period in consenting participants. Tophi were assumed to be absent if not documented in the medical notes. Where multiple readings of SUA were available, only the highest recorded value in the preceding two years was included in the study. SUA was considered as not checked in the absence of a documented value.

5.4.4 Missing data

The completeness of HRQOL data was ascertained from item non-response for the GIS, PF-10 and HAQ-DI. Scoring the HAQ-DI using the standard disability index method takes into account the use of aids or devices and help from another person (Bruce, Fries 2003a). These items of the HAQ-DI however have a single tick box response option. If left unchecked, it is assumed that no adjuncts or help is needed (rather than data missing). In order to calculate the mean HAQ-DI, at least 6 out of the 8 categories needed to have a score (Bruce, Fries 2003a). For the PF-10, answers to each of the 10 questions are summed to give a final score which is transformed to a 0 to 100 scale (White, Wilson et al. 2011). For the GIS sub-scales, mean scores were calculated if at least half the items within the sub-scale were answered (Hirsch, Lee et al. 2008). For self-reported gout and socio-demographic characteristics, the data were considered missing if the response option(s) were left blank or unticked. In order to calculate the frequency of missing data for the dose of allopurinol, only those participants who reported treatment with allopurinol were considered as the denominator. Similarly missing data for age at which further education ended was only relevant in participants who had reported attendance at a higher education institution. For co-morbid characteristics, an unselected response option (single tick box) signified the absence of the co-morbidity rather than missing data.

5.4.5 Analysis

All descriptive statistics pertaining to aims and objectives in this chapter were calculated in SPSS (Version 21.0. IBM Corp). The flow of the participants through the cross-sectional study was described using descriptive statistics (frequency and percentages). The number of mailed, responders, non-responders, refusals and consenters for medical record review were ascertained from the study mailing database. The numbers excluded and refusals for specific reasons were obtained from study accrual.

Response bias was described using socio-demographic data obtained from general practice records. Age, gender and MDI rankings were stored in the study demographics database. Age and neighbourhood deprivation were treated as ordinal data and gender as nominal. These socio-demographic characteristics were described using simple descriptive statistics (frequency and percentage) for the mailed study population and further grouped by responders and non-responders.

For survey responders, descriptive statistics (frequency and percentage, mean and standard deviation or median and interquartile range depending upon the distribution of variables) were presented for co-morbidities (hypertension, hyperlipidaemia, diabetes, renal calculi, renal failure, MI, angina, TIA, stroke, anxiety, depression, body pain and BMI), frequency of alcohol intake (6 response options ranging from never to daily) and gout-related characteristics (frequency of attack over the preceding 12 months, currently having an attack of gout, history of oligo or polyarticular attacks, treatment with allopurinol, dose of allopurinol, disease duration). These characteristics were ascertained from the study questionnaire database which stores the self-reported questionnaire data.

Missing data for self-reported responder characteristics was presented as frequency and percentages. An unselected dichotomous or categorical response option for all gout, socio-demographic (relationship status, ethnicity, attendance at further education and age at which further education left, alcohol consumption) and body pain were assumed as missing data. Itemised missing data (range) was provided for PHQ-9, GAD-7, PF-10, HAQ-DI and GIS sub-scales. Generally an unselected single response option was indicative of the absence of the condition (medical co-morbidity, aids/devices and help from another person in the HAQ-DI) with the exception of missing height and weight. If unanswered, height and weight were considered missing. Although unlikely, missing data from general practice records for age, gender, MDI neighbourhood deprivation was also assessed. Tophi (present or absent) and SUA (test performed or not performed) were ascertained from medical record review and were not considered to have missing values.

5.5 Results

5.5.1 Survey response

Of the 1805 participants eligible to participate in the study, 1796 were deemed suitable for the mailing process - 9 participants were excluded due to ill health, death or departures from the general practice. Of the 1796 mailed participants, 1184 returned the completed questionnaire (adjusted response 65.9%⁶). Overall, 612 participants did not provide completed questionnaires either due to non-response (517 (28.8%)) or withdrawal from the survey (95 (5.3%)). Those who had withdrawn from the survey had contacted the study team and asked to be exempted (not having gout cited as a reason by 43, poor health by 9 and no reason given by 43). Two participants withdrew from the study after questionnaire completion. Hence there are 1184

⁶ Adjusted response calculated based on a denominator of 1796 participants who were mailed a questionnaire.

participants in the database that stores questionnaire responses but only 1182 in the database that determines future mailings. 1079 (91.9 %) of the 1184 baseline responders consented to medical record review. Breakdown of the survey response is summarised in flowchart (Figure 6).

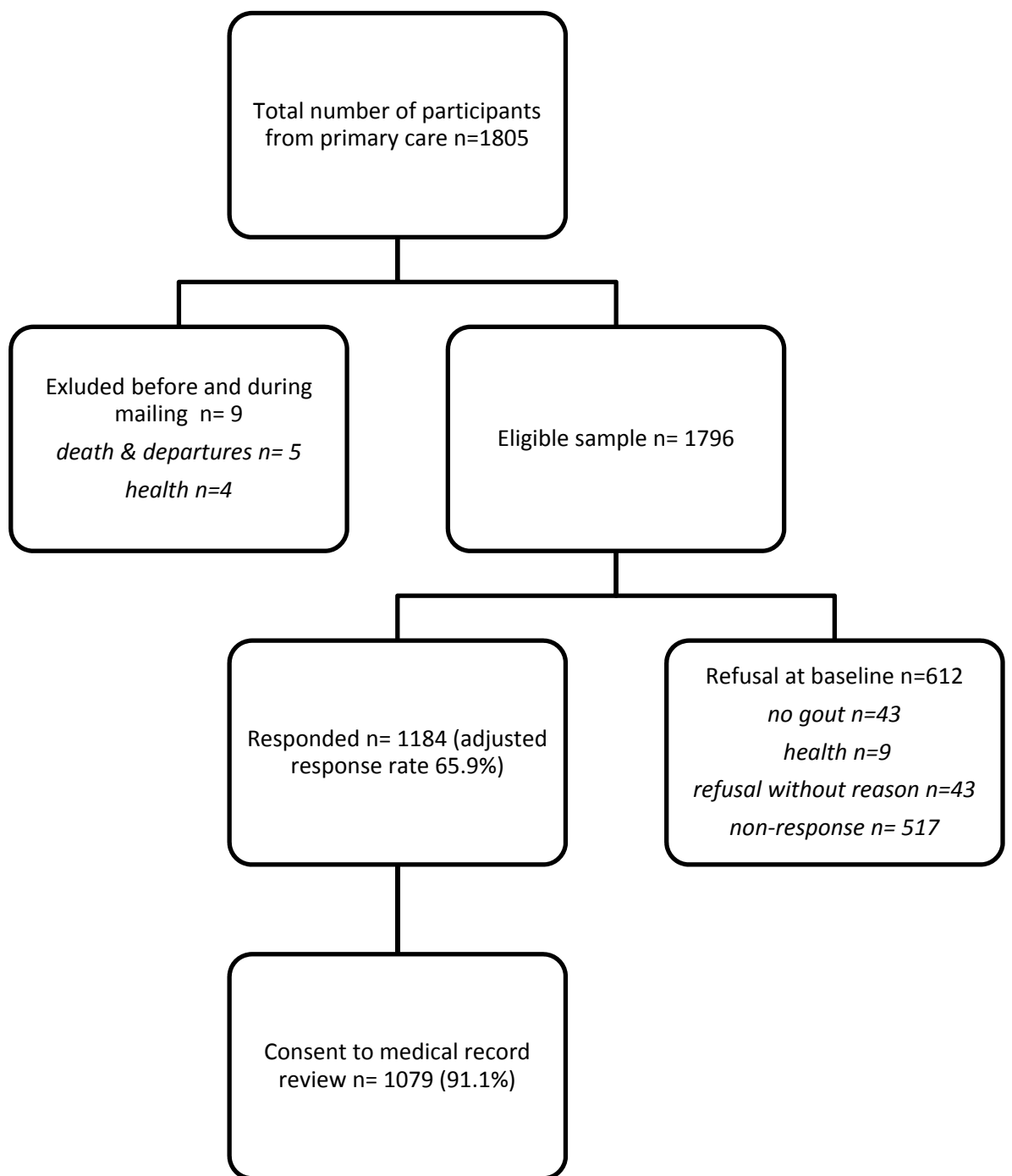


Figure 6: Flow diagram of participants in the cross-sectional study

5.5.2 Differences between survey responders and non-responders

Response bias was assessed by examining the socio-demographic differences between responders and non-responders. Simple descriptive statistics (frequency and percentage) were calculated for age, gender and MDI rank quintiles, as shown in Table 5-1. Of all the responders, a greater proportion were male (83.6%). A greater proportion of non-responders were females (22.2%) compared to responders (16.4%). Both male and female responders were older than non-responders, with greater proportions over the age of 60. Responders were more likely than non-responders to live in the least deprived areas (see Table 5-1).

Table 5-1: Differences between responders and non-responders to the cross-sectional survey

		All mailed, n (%)	Responders, n (%)	Non-responders and refusals, n (%)
n		1805 ⁷	1184	612
Male		1471 (81.5)	990 (83.6)	476 (77.8)
Female		334 (18.5)	194 (16.4)	136 (22.2)
Age (years)	<40	80 (4.4)	26 (2.2)	53 (8.7)
	40-49	228 (12.6)	116 (9.8)	111 (18.1)
	50-59	348 (19.3)	210 (17.7)	137 (22.4)
	60-69	480 (26.6)	343 (29.0)	136 (22.2)
	70-79	448 (24.8)	339 (28.6)	107 (17.5)
	≥ 80	221 (12.2)	150 (12.7)	68 (11.1)
Age (years), Males	<40	78 (5.3)	25 (2.5)	52 (10.9)
	40-49	216 (14.7)	113 (11.4)	103 (21.6)
	50-59	301 (20.5)	187 (18.9)	113 (23.7)
	60-69	401 (27.3)	293 (29.6)	108 (22.7)
	70-79	340 (23.1)	273 (27.6)	65 (13.7)
	≥ 80	135 (9.2)	99 (10.0)	35 (7.4)
Age (years) Females	<40	2 (0.6)	1 (0.5)	1 (0.7)
	40-49	12 (3.6)	3 (1.5)	8 (5.9)
	50-59	47 (14.1)	23 (11.9)	24 (17.6)
	60-69	79 (23.7)	50 (25.8)	28 (20.6)

⁷ 9 of these participants excluded during the mailing process

		All mailed, n (%)	Responders, n (%)	Non-responders and refusals, n (%)
	70-79	108 (32.3)	66 (34.0)	42 (30.9)
	≥ 80	86 (25.7)	51 (26.3)	33 (24.3)
Neighbourhood deprivation ⁸	Most deprived	362 (20.1)	208 (17.6)	152 (24.8)
	Second most deprived	357 (19.8)	241 (20.4)	118 (19.3)
	Mid-deprived	363 (20.1)	238 (20.1)	121 (19.8)
	Second least deprived	354 (19.6)	240 (20.3)	115 (18.8)
	Least deprived	368 (20.4)	257 (21.7)	105 (17.2)

⁸ Data missing for 1 participant

5.5.3 Characteristics of survey responders

5.5.3.1 *Gout-specific characteristics*

The mean (SD) number of attacks over the preceding 12 months was 1.7 (1.7) with 397 participants (33.5%) having no attacks during this time period (see Table 5-2). This data however was skewed towards lower frequency of attacks (see appendix 18). The median number of attacks in the preceding 12 months was 1 (interquartile range, IQR 0 to 3). 493 (41.6%) participants had ≥ 2 attacks over the preceding 12 months (of these, only 242 (49.1%) reporting taking allopurinol, data not shown in Table 5-2). 132 participants (11.1%) expressed having an acute attack of gout at the time of questionnaire completion and 435 (36.7%) had ever experienced an attack of gout in more than one joint (oligo or polyarticular attacks). The mean (SD) disease duration was 11.9 (12.1) years. Overall, 630 participants (56.3%) were receiving urate-lowering treatment with allopurinol. The median (IQR) dose of allopurinol taken was 300 mg (100 mg to 300 mg). The highest recorded serum uric acid in the 2 years preceding the study and the presence of tophi were ascertained from medical record review of 1079 (91.1%) of responders who consented to medical record review. Only 108 out of the 461 (23.4%) who had SUA recorded achieved the target level of SUA $< 360 \mu\text{mol/L}$. The mean (SD) serum uric acid was $441.4 (115.5) \mu\text{mol/L}$. When grouped by treatment with or without allopurinol, 23.9% and 35.9% responders had a SUA $> 360 \mu\text{mol/L}$ respectively (data not shown in Table 5-2). 25 (2.3%) responders who consented to medical record review had the presence of tophi documented in the record.

5.5.3.2 *Co-morbid conditions*

The commonest self-reported co-morbidities were hypertension (n= 730, 61.7%), hyperlipidaemia (n= 508, 42.9%), diabetes mellitus (n= 205, 17.3%), angina (n= 147, 12.4%) and myocardial

infarction (n= 119, 10.1%) (see Table 5-2). Renal diseases (renal calculi n= 81, 6.8%, renal failure, n= 56, 4.7%) and cerebro-vascular diseases (TIA n= 62, 5.2% and stroke n= 37, 3.1%) were less commonly reported. The median (IQR) BMI was 28.3 (25.5 to 31.6). Pain affecting any part of the body and lasting greater than 24 hours in the past month was reported by 650 (55%) of the participants. Anxiety and depression were reported by 141 (11.9%) and 148 (12.5%) participants respectively.

5.5.3.3 Socio-demographic characteristics

The mean age (SD) of survey responders was 65.6 (12.5) years. The majority were male (83.6%) and Caucasian (95.1%). Daily alcohol intake was reported by 272 (23%) participants whereas 113 (9.5%) refrained from drinking alcohol altogether. The majority (n= 921, 77.8%) of responders were married or shared accommodation with another person. Only a minority (n= 249, 21%) pursued further education after school.

Table 5-2: Characteristics of the survey responders

Variable	N (%)
Age (years), mean (SD)	65.6 (12.5)
Male	990 (83.6)
Married or cohabiting	921 (77.8)
Attended further education	249 (21.0)
Caucasian ethnicity	1126 (95.1)
Gout characteristics	
Attack frequency in 12 months, mean (SD)	1.7 (1.7) ⁹
Attack frequency in the past 12 months	
0	397 (33.5)
1	231 (19.5)
2	187 (15.8)
3	102 (8.6)
4	67 (5.7)
>=5	137 (11.6)
Currently having an attack of gout of gout	132 (11.1)
Oligo or polyarticular attack	435 (36.7)
Treatment with allopurinol	630 (56.3)
Allopurinol dose (mg), median (IQR)	300 (100 – 300)
Tophi present ¹⁰	25 (2.3)
SUA (μmol/L), mean (SD) ¹¹	441.4 (115.5)
Disease duration (years), mean (SD)	11.9 (12.1)
Co-morbid conditions	
Hypertension	730 (61.7)
Body pain	650 (55.0)
Hyperlipidaemia	508 (42.9)
Diabetes	205 (17.3)
Angina	147 (12.4)
Myocardial infarction	119 (10.1)
Renal calculi	81 (6.8)
TIA	62 (5.2)
Renal failure	56 (4.7)
Stroke	37 (3.1)
BMI, median (IQR)	28.3 (25.5 – 31.6)
Anxiety	
None	842 (71.1)

⁹ Median 1, IQR 0 to 3¹⁰ Tophi and SUA ascertained from medical records of 1079 consenting participants.¹¹ In 461 participants with one or more recorded SUA

Variable	N (%)
Mild	141 (11.9)
Moderate	64 (5.4)
Severe	45 (3.8)
Depression	
None/minimal	761 (64.3)
Mild	148 (12.5)
Moderate	65 (5.5)
Moderately severe	40 (3.4)
Severe	26 (2.2)
Lifestyle	
<i>Alcohol intake</i>	
Daily	272 (23.0)
3-4 times per week	262 (22.1)
1-2 times per week	254 (21.5)
1-3 times per month	109 (9.2)
Special occasions	155 (13.1)
Never	113 (9.5)

Abbreviations: SD: Standard Deviation; IQR: Interquartile Range; BMI: Body Mass Index; SUA: Serum Uric Acid; mg: Milligrams; $\mu\text{mol/L}$: micromoles per litre.

5.5.4 Missing data

The frequency of missing data for self-reported gout, socio-demographic characteristics, body pain, psychological co-morbidities and quality of life are listed in Table 5-3. The level of missing data for self-reported gout characteristics (currently having an attack of gout, frequency of attack, oligo or polyarticular attacks, treatment with allopurinol, age at diagnosis of gout) ranged from 4% to 8%. Less than 6% of data was missing for socio-demographic characteristics (ethnicity, attendance at further education, age at leaving further education, relationship status, alcohol intake, height, weight and neighbourhood deprivation indices). The highest frequency of missing socio-demographic data was for attendance at further education (5.7%) followed by weight (3.8%). The GAD-7 questionnaire had missing data ranging from 4.8% to 5.5% (see Table 5-3). PHQ-9, had missing data ranging from 5.4% to 7.3%. Data pertaining to pain affecting any part of the body was missing in 18.3% of the responders.

Missing data for the items of PF-10 ranged from 2.2% (bathing and dressing) to 3.7% (vigorous activities). For the items of HAQ-DI, the range of missing data was higher, from 3.6% (opening car door) to 15.5% (taking a bath). Less than 5% of the data for gout-specific HRQOL in the GIS CO was missing, compared to 5% (bothered by medication side-effects) to 9% (medications do not work well to prevent attacks) for the treatment sub-scales. Whereas 2.6% (ability to do what you want) to 13.6% (miss work due to gout symptoms) data were missing for wellbeing during attack, approximately 4% were missing for concern during attack.

Table 5-3: Frequency and percentage of missing data for independent and dependent variables

Variable	Missing data n (%)
Gout characteristics	
Current gout attack	51 (4.3)
>1 joint involvement	55 (4.6)
Number of gout attacks in the last 12 months	63 (5.3)
Currently taking allopurinol	66 (5.6)
Allopurinol dose (mg) ¹²	33 (5.3)
Age at gout diagnosis (years)	88 (7.4)
Co-morbidities	
GAD-7	
Feeling afraid something awful may happen	65 (5.5)
Worrying too much	57 (4.8)
Easily annoyed / irritable	58 (4.9)
Nervous / anxious	62 (5.2)
Not being able to stop or control worrying	65 (5.5)
Trouble relaxing	58 (4.9)
Restless	65 (5.5)
PHQ-9	
Little interest	69 (5.8)
Feeling down	79 (6.7)
Sleep problems	80 (6.8)
Feeling tired	64 (5.4)
Poor appetite/overeating	86 (7.3)
Feeling bad	79 (6.7)
Trouble concentrating	67 (5.7)
Moving/speaking slowly / restlessness	74 (6.3)

¹² Those who reported treatment with allopurinol (n= 628) used as denominator

Variable	Missing data n (%)
Better off dead	73 (6.2)
Generalised body pain	217 (18.3)
Socio-demographic characteristics	
Relationship status	21 (1.8)
Attended further education	67 (5.7)
Age left full time education ¹³	9 (3.2)
Ethnicity	32 (2.7)
Alcohol frequency	19 (1.6)
Neighbourhood deprivation status (quintiles)	1 (0.1)
Height	28 (2.4)
Weight	45 (3.8)
Health Related Quality of Life	
PF-10	
Vigorous activities	44 (3.7)
Moderate activities	29 (2.4)
Lifting or carrying	29 (2.4)
Several flights of stairs	36 (3.0)
One flight of stairs	34 (2.9)
Bending, kneeling or stooping	29 (2.4)
Walking > 1 mile	35 (3.0)
Walking 1/2 mile	38 (3.2)
Walking 100 yards	31 (2.6)
Bathing & dressing	26 (2.2)
HAQ-DI	
Dress yourself	69 (5.8)
Shampoo your hair	76 (6.4)
Stand from chair	55 (4.6)

¹³ Those who attended further education (n=248) used as denominator

Variable	Missing data n (%)
Get in & out of bed	56 (4.7)
Cut your meat	58 (4.9)
Open a milk carton	54 (4.6)
Lift full glass or cup to your mouth	47 (4.0)
Walk outdoors on flat ground	52 (4.4)
Climb up 5 steps	67 (5.7)
Wash & dry entire body	61 (5.2)
Take a bath	183 (15.5)
Get on & off toilet	46 (3.9)
5lb bag from above head	78 (6.6)
Open car doors	43 (3.6)
Open previously opened jars	48 (4.1)
Bend to pick clothing from floor	63 (5.3)
Turn taps on & off	52 (4.4)
Run errands & shop	118 (10.0)
Get in & out of car	44 (3.7)
Do chores	95 (8.0)
GIS CO	
Worried will have attack in next 12/12	48 (4.1)
Afraid that gout will get worse	41 (3.5)
Worry won't be able to enjoy leisure activities	44 (3.7)
Anxious gout will interfere with future activities	45 (3.8)
GIS MSE	
Bothered by side-effects of medications	63 (5.3)
Worry about long-term effects of gout medications	68 (5.7)
GIS UTN	
Current medications effective at treating an attack	79 (6.7)
Current medications do not work well to prevent attacks	106 (9.0)

Variable	Missing data n (%)
I have control over my gout	72 (6.1)
GIS WBDA	
Miss work because of symptoms	161 (13.6)
Difficulty working because of symptoms	136 (11.5)
Difficulty with social activities because of symptoms	40 (3.4)
Difficulty with self-care because of symptoms	33 (2.8)
Mood	43 (3.6)
Ability to move about	33 (2.8)
Sleep	39 (3.3)
Normal work	67 (5.7)
Recreational activities	51 (4.3)
Enjoyment of life	37 (3.1)
Do what you want	31 (2.6)
GIS CDA	
Angry when experience attack	56 (4.7)
Difficult to plan ahead	46 (3.9)
Depressed when get an attack	53 (4.5)
Miss planned/important activities when have attack	53 (4.5)

Abbreviations: PF-10: Physical Function 10; HAQ-DI: Health Assessment Questionnaire Disability Index; GIS CO: Gout Impact Scale Concern Overall; MSE: Medication Side effects; UTN: Unmet Treatment Need; WBDA: Well-being During Attack; CDA: Concern During Attack; GAD-7: Generalised Anxiety Disorder; PHQ-9: Patient Health Questionnaire.

5.6 Discussion

This chapter described the response to the survey, the socio-demographic differences between responders and non-responders, and the gout-specific and co-morbid characteristics of survey responders. The adjusted response rate for this study was 65.9% and the majority of responders (83.6%) were males. Responders were more likely to be male, older and live in less deprived areas than non-responders. Majority of the responders were of Caucasian ethnicity (95.1%). The mean number of attacks of gout over the preceding 12 months was 1.7 although just over a third had experienced no attacks at all during this period. 435 (36.7%) responders reported a history of oligo or polyarticular attacks. Approximately half of the responders were on urate-lowering treatment with allopurinol (median dose 300 mg per day). The mean SUA (441 $\mu\text{mol/L}$) was above the physiological saturation threshold of uric acid in the body tissues (360 $\mu\text{mol/L}$) (Edwards 2008) (Zhang, Doherty et al. 2006b). Co-morbid conditions such as hypertension, hyperlipidaemia and diabetes were commoner than other self-reported conditions. Just over 10% of responders reported symptoms of mild anxiety (measured by GAD-7) and depression (measured by PHQ-9). Approximately a quarter of the responders reported daily consumption of alcohol.

A response of 65.9% in this study was considered reasonable as in a postal survey there is no consensus as to what is an acceptable value. Some consider a response of $\geq 70\%$ to be acceptable (Fowler, Mangione 1990) and $\leq 30\%$ to be of no value in providing valuable information (Moser, Kalton 1971). Response boosting strategies (reminder post card and letter accompanied by a repeat questionnaire) were used in this study in keeping with the standard operating procedures of the research centre. However other strategies to improve postal survey response rates include reducing the length of the questionnaire (Edwards, Roberts et al. 2004), providing incentives to participants (Phil Edwards, Ian Roberts et al. 2002), use of coloured papers and inks (McColl,

Jacoby et al. 2001). Shortening the length of the questionnaire may have been difficult in this study as the main aim was to assess the association of gout with HRQOL (gout-specific and generic) independent of co-morbidities and socio-demographic characteristics. There remains a lack of consensus regarding the use of thicker quality paper, illustrations within the questionnaires and printing the questionnaire using dot matrix compared to letter quality print in boosting response rates ((Phil Edwards, Ian Roberts et al. 2002).

Response bias was examined using demographic data (age, gender and neighbourhood deprivation ranking calculated from post code) for the responders as well as non-responders. Males were over-represented in the overall response but were representative of the age distribution of the mailed study population. The demographic findings reflect the predilection of gout for males (fourfold increase in the rate of gout prevalence in males) (Khanna, Ahmed et al. 2008) and older persons (Doherty 2009) and is in keeping with findings of other studies (Hirsch, Lee et al. 2008; Colwell, Hunt et al. 2006; Hirsch, Terkeltaub et al. 2010). The pre-dominantly Caucasian population in the study reflects the demographic composition of the area surveyed (82.7% of the population is Caucasian in the West Midlands¹⁴). Low response rates from deprived neighbourhoods may be a consequence of low health literacy, disengagement (lack of insight into the disease and perceived lack of benefit to self from participation in the survey) (Sheldon, Graham et al. 2007) and social desirability bias (although more common in interviews compared to postal surveys, potential participants may be unwilling to participate due to the stigma attached with unemployment or lifestyle factors) (Bowling 2005).

¹⁴ <http://www.nomisweb.co.uk/census/2011/KS201EW/view/2013265925?cols=measures>

Although unmeasured, the disease characteristics of survey non-responders may differ systematically from responders. For example, the uptake of allopurinol in this study (56.3%) is higher than the 28% to 46% uptake reported by previous UK based primary care studies (Roddy, Zhang et al. 2007c; Roddy, Zhang et al. 2007b; Harris, Lloyd et al. 1995; Kuo, Grainge et al. 2014). In fact the uptake of allopurinol in this study is similar to that reported in secondary care (between 52% and 56%) (Lee, Hirsch et al. 2009; Khanna, Ahmed et al. 2008). This may indicate that compared to non-responders, study responders may have a more severe form of gout that needs treatment with allopurinol. Those with severe disease (treated with allopurinol) compared to those with milder disease (untreated with allopurinol) may be more inclined to participate in such study, therefore causing response bias. On the other hand, it is plausible that participants report over-adherence to treatment in a self-administered questionnaire (Mosley-Williams, Lumley et al. 2002; Harrold, Andrade 2009) as they believe this is what the researchers want to hear (Choo, Rand et al. 2001; Cornwell 1984; Myers, Midence 1998). Other risk factors for over-reporting include frequent daily dosing and perception of low risk from treatment non-adherence (Choo, Rand et al. 2001), both of which may be true in the case of allopurinol use.

Alternatively those on allopurinol may have better disease (symptom) control, enabling them to participate in the study. Other indicators of less severe or better controlled disease in study responders include approximately a third of the participants reporting no attacks in the last 12 months, only a third of the participants reporting a history of oligo or polyarticular attacks, only 11% reporting experiencing an acute attack at the time of questionnaire completion and the low prevalence of tophi.

Just over a third (33.5%) of the responders reported not having an acute attack of gout in the last 12 months at the time of questionnaire completion, in contrast to mixed primary and secondary

care community validation studies of the GIS which report 19.6% participants not having an attack in the past 12 months (Hirsch, Lee et al. 2008; Hirsch, Terkeltaub et al. 2010). Approximately a third (36.7%) of the responders reported a history of oligo or polyarticular attacks of gout, indicative of less severe disease when compared to a prevalence of oligo or polyarticular gout in 88.9% of participants in secondary care (Khanna, Perez-Ruiz et al. 2011). The prevalence of tophi (2.3%) amongst the responders was lower than that reported previously in UK primary care (6%) (Roddy, Zhang et al. 2007b) and international mixed primary and secondary care studies (up to 40%) (Hirsch, Lee et al. 2008; Hirsch, Terkeltaub et al. 2010; Dalbeth, Petrie et al. 2011 and Khanna, Perez-Ruiz et al. 2011). Differences between the findings of this study and those of others may be attributable to differences in the study setting and methods of data ascertainment. Data was gathered through a comprehensive clinical assessment in other studies (Roddy, Zhang et al. 2007b; Dalbeth, Petrie et al. 2011; Khanna, Perez-Ruiz et al. 2011) as opposed to self-reported and ascertained from medical records in ours. Restricting participation to those with crystal proven diagnosis of gout (Khanna, Perez-Ruiz et al. 2011) or presence of tophi (Alvarez-Hernandez, Zamudio-Lerma et al. 2009) in secondary care specialist clinics may also explain the differences in disease severity seen between this and other study samples. Finally geographical variation in disease severity may also explain the differences in findings of this and other studies. A greater prevalence of polyarticular and tophaceous gout has been recognised in those of Maori ethnicity compared to those of European ethnicity (Klemp, Stansfield et al. 1997), tophi and involvement of upper limbs were reported as presenting features in the face of an overall increasing prevalence of gout in the USA (Wallace, Riedel et al. 2004; Arromdee 2002).

Although participants in this study have higher reported use of allopurinol compared to other studies, only half of those with an attack frequency of ≥ 2 in the preceding 12 months were on allopurinol, which is not concordant with national (British Society for Rheumatology, BSR (Jordan,

Cameron et al. 2007)) or international (American College of Rheumatology, ACR (Khanna, Fitzgerald et al. 2012) and European League against Rheumatism, EULAR (Zhang, Doherty et al. 2006a)) guidelines. Although not the primary aim of this study, our results provide further evidence that gout is sub-optimally treated in primary care in the UK (Pal, Foxall et al. 2000; Roddy, Zhang et al. 2007b; Cottrell, Crabtree et al. 2013) as the mean SUA for participants remains largely over the threshold of urate crystal saturation ($360\text{ }\mu\text{mol/L}$). Only 23.4% of our participants have SUA below the target level ($360\text{ }\mu\text{mol/L}$), a finding replicated in a cluster analysis of co-morbidities in France (22.3%)(Richette, Clerson et al. 2013). However when restricted to those on allopurinol, only 23.9% of the responders had a SUA $> 360\text{ }\mu\text{mol/L}$, which is almost the same (23%) as that seen in the study of two UK general practices (Roddy, Zhang et al. 2007b). By contrast, 35.9% of those not treated with allopurinol have a SUA $> 360\text{ }\mu\text{mol/L}$. Despite being effective in reducing SUA, findings from this study indicate that allopurinol dose is not titrated upwards appropriately. Compared to 47.8% in this study, 70% of responders in a survey of two UK general practices were on allopurinol 300 mg per day (Roddy, Zhang et al. 2007b). Only 3.8% of responders in this study were on doses $> 300\text{ mg}$ per day whilst 43.3% were on $< 300\text{ mg}$. Such finding however is not unique - in a retrospective analysis of US managed care database, $<5\%$ received allopurinol $> 300\text{ mg}$ per day and $> 30\%$ received $< 300\text{ mg}$ (Sarawate, Brewer et al. 2006).

Despite the varying severity of gout, the prevalence of co-morbid conditions remains similar in this and other studies. As seen in this sample, hypertension (74%) and hyperlipidaemia (58.8%) were also the commonest co-morbidities in other primary and secondary care studies (Hirsch, Lee et al. 2008; Roddy, Zhang et al. 2007c; Lioté, Lancrenon et al. 2012). The prevalence of renal failure was reported as higher than that found previously in a UK primary care study of gout (Roddy, Zhang et al. 2007c) but lower than prevalence of 'kidney problems' (35.6%) reported by

participants in the mixed primary and secondary care study by Hirsch et al (Hirsch, Lee et al. 2008). Kidney problem is a term likely to be more widely recognised by participants and encompasses chronic kidney disease, which was not included in this survey. The prevalence of at least mild anxiety and depression (between 12% to 13%) are variable when compared to findings in existing studies, which are nested within larger studies and use different means to assess anxiety. In the US based National Health and Nutrition Examination Survey (NHANES 2009- 2010), the prevalence of depression assessed by the PHQ-9 in those aged ≥ 60 with gout was 13.5% (95% CI, 7.7 to 22.5%)(Ege, Messias et al. 2013). The prevalence of anxiety (using the HADS cut-off ≥ 8) in 50 patients with gout in a Singapore based study (nested within a cross-sectional and a cohort study) was 6% (Mak, Tang et al. 2011).

5.6.1 Strengths of the study

The similarities between gout (frequency of attack in the last year, prevalence of tophi, uptake of allopurinol, SUA) and demographic characteristics (predilection of gout for overweight males) in this study and other primary care studies suggests that the findings are representative of gout managed in UK primary care. Given that 98% of the UK population are registered with a general practice (Bowling 2009) and gout is most commonly diagnosed and managed in the general practice, setting the study in primary care ensures that the findings are generalizable to most patients with gout. Strategies for identification of participants with gout were considered robust as the participating general practices undergo regular audits by the Primary Care Research Network (PCRN) team to ensure adequate quality and completeness of data entry (Porcheret, Hughes et al. 2004). Although possible that participants may report data in a way they perceive more acceptable to the investigators (Hennekens, Buring et al. 1987) (under-reporting of alcohol consumption and over-reporting the uptake of allopurinol), previous studies undertaken in those with chronic diseases have shown acceptable concordance between self-reported and medical

record data, particularly medication use, anthropometric and demographic data (Tisnado, Adams et al. 2006; Zhu, McKnight et al. 1999). Using electronic medication event monitors which register the opening of medication package, the compliance with 'taking ULT' was 84%, 'correct dosing' 74% and 'timing' 65% (de Klerk, van der Heijde et al. 2003). In the Artherosclerosis Risk in Communities (ARIC) and Campaign Against Cancer and Heart Disease (CLUE II) cohorts, the sensitivity of self-reported physician diagnosis of gout against a hospital discharge diagnosis of gout or prescription of gout medication (84%) and reliability at repeated follow-up time-points (65%) were deemed adequate for population based studies (McAdams, Maynard et al. 2011). Concordance between self-reported and prescription of anti-depressant use was seen in 85% of cases, with a kappa of 0.69 (Kwon, Bungay et al. 2003). It may be that self-reported data more accurately reflects the indication for medication use compared to medical records (which may identify medication use for condition other than that under investigation) (Kwon, Bungay et al. 2003).

Other quality assurance processes included checking the contact details of participants (name, date of birth, address) in the completed questionnaires against the information obtained from the general practice records (mailing database) to ensure that the intended person had completed the questionnaire.

5.6.2 Limitations of the study

The generalizability of the study findings to females, racially diverse geographical areas and those living in deprived neighbourhoods should be interpreted with some caution. Although cost-effective, suitable for covering a diverse geographical area (as in this cross-sectional study) and relatively protected from investigator bias, postal surveys can be susceptible to selective item non-response and completion by proxy (Armstrong, White et al. 1995). Non-response to the

HAQ-DI item taking a tub bath (hygiene category) was seen in 15.5% of the participants. However related activities such as shampooing or drying the body had much lower levels of missing data (4% to 6%). Ability to take a bath was also included in the PF-10 but the level of missing data was much lower (2.2%). Responders to this survey had a mean age of 65 years and it is plausible that many do not have a tub bath at home due to reduced physical agility and hence the question was not relevant to them. Similarly responders at the age of 65 years or over who are likely to be retired may not find questions regarding employment relevant. This possibility is supported by the higher levels of missing data (>10%) seen for the two work related questions in the wellbeing during attack sub-scale of the GIS. Nevertheless these questions are an integral part of the validated questionnaires that comprise the survey and hence their inclusion was deemed justified. The diagnosis of gout was ascertained from Read Code entries by GPs (or prescription of colchicine or allopurinol). The method of diagnosis in primary care was not ascertained. The diagnosis could be dependent upon the clinician's judgement which may or may not include one or more of the clinical composite of rapid onset of pain, swelling, erythema reaching peak intensity within 6 to 12 hours or the classical presentation of podagra and hyperuricaemia (Zhang, Doherty et al. 2006b). Although gold standard, identification of MSU crystals from synovial fluid remains uncommon in primary care (Roddy, Zhang et al. 2007c). The accurate diagnosis of self-reported gout in primary care however has been substantiated previously – as many as 83% of self-reported diagnosis of gout were considered appropriate after assessment by a specialist using the American Rheumatism Association (ARA) criteria (Roddy, Zhang et al. 2007b; Wallace, Robinson et al. 1977). A study of prescription and co-morbidity screening following a consultation for acute gout demonstrated that free text entries describing the features of inflammation and joint pattern involvement in the Consultation in Primary Care Archive (CiPCA) database are concordant with a diagnosis of gout (Roddy, Mallen et al. 2010). SUA ascertained from medical records was not recorded for 723 (42.7%) participants. The prevalence of tophi was only 2.3%(n =25) from medical record review. It is possible that tophi are under-diagnosed in a

non-specialist setting and their similarity to (and hence misdiagnosis as) rheumatoid nodules has been previously noted (Schlesinger 2005).

5.6.3 Implications for clinical practice and further research

As the response was considered acceptable (65.9%) and majority of responders were male and Caucasian with an average age of 65 years, the findings are representative of people with gout managed in primary care and may have implications for primary care practice. The predilection of gout for middle aged or older men and its association with co-morbidities such as the metabolic syndrome and diabetes imply that in clinical practice, a high index of suspicion should be maintained towards gout in those with symptoms of acute synovitis and above risk factors. Conversely, it may be appropriate to screen for these and other associated co-morbidities (such as anxiety and depression) during a routine consultation for gout. Approximately a quarter of those treated with allopurinol had a SUA > 360 $\mu\text{mol/L}$, which represents an unmet need for upwards titration of allopurinol dose in practice. Only half of those with an attack frequency of ≥ 2 in the preceding year were on allopurinol in this study, which is not concordant with current guidelines (Jordan, Cameron et al. 2007; Khanna, Fitzgerald et al. 2012; Zhang, Doherty et al. 2006a) and provides evidence for more widespread use of allopurinol in practice. Given the self-reported daily consumption of alcohol by approximately a quarter of the responders and the median BMI of 28, lifestyle modification should be advocated as an adjunct to pharmacological treatment.

Although based in a non-selective primary care population, this study has a small proportion of female and non-Caucasian participants. Future research nested within these two groups will help fill in the gaps in the existing knowledge about how gout affects these population groups. A sub-sample of self-reported data (co-morbidities for example) could be triangulated against medical

record review of consenting participants in future research projects, to check the accuracy of self-reported data. Similarly, clinical assessment of participants by a physician trained in diagnosing gout to accurately ascertain the presence of tophi and measurement of SUA at the time of questionnaire completion add to the accuracy of data obtained from review of general practice records.

5.7 Conclusion

The results in this chapter highlighted the flow of participants through the study, their response, gout-specific, co-morbid and socio-demographic characteristics. It also outlined the key strengths of the findings of this study such as adequate response, representativeness of the study participants of those with gout in primary care and participant characteristics consistent with those found in previous studies. This chapter also acknowledged its limitations, primarily pertaining to missing data in the questionnaires or uncertainty about the accuracy of data obtained from medical record review (low prevalence of tophi and high frequency of unrecorded SUA). The next chapter considers how survey responders' gout, co-morbid and socio-demographic characteristics affect their HRQOL. The next chapter in the thesis will look at HRQOL scores for participants grouped by the above characteristics.

6 The association of gout, co-morbid and socio-demographic characteristics with Health Related Quality of Life: Univariate analysis

6.1 Introduction

The previous chapter described the survey response and socio-demographic differences between survey responders and non-responders. It also described the gout-specific and co-morbid characteristics of survey responders. This chapter aims to describe the association of Health Related Quality of Life (HRQOL) with these characteristics through univariate analysis. The differences in mean HRQOL scores grouped by participant characteristics will be examined. HRQOL will be assessed through the generic questionnaire namely the Physical Function 10 (PF-10) and Health Assessment Questionnaire Disability Index (HAQ-DI) and the gout-specific questionnaire, the Gout Impact Scale (GIS).

6.2 Objectives

- I. To define gout, co-morbid and socio- demographic characteristics of respondents by dichotomous or categorical outcomes
- II. To describe the mean (standard deviation) or median (interquartile range) scores of HRQOL (PF-10, HAQ-DI and GIS) stratified by gout-specific, co-morbid and socio-demographic characteristics

6.3 Methods

Data in this chapter is obtained from the baseline phase of the primary care-based cohort study of HRQOL in gout and medical record review of consenting participants. The sampling frame (study inclusion and exclusion criteria), recruitment of study participants (initiating contact and mailing

procedures) and questionnaire contents have been described in detail in chapter 4 (Study design and methods).

6.3.1 Gout characteristics

The frequency of attacks in the preceding 12 months was ascertained using six response options (0, 1, 2, 3, 4, ≥ 5). Disease duration was calculated from the age at the diagnosis of gout in years. A current attack of gout, a history of oligo or polyarticular attacks of gout and treatment with allopurinol were ascertained using a 'yes' or 'no' response. Those participants who reported treatment with allopurinol were asked to tick a box corresponding to the dose (11 response options ranging from 50 mg to 900 mg and unknown) or write the dose in a free text box should it not be covered in the response options. Tophi (present or absent) and serum uric acid (SUA) (recorded or not recorded) in the 2 years preceding the study were ascertained from medical record review of consenting participants. When more than one recorded SUA was available, the highest value was included in the study.

6.3.2 Co-morbid conditions

The following medical co-morbidities were ascertained using a single tick box response option indicating their presence (or absence if left unticked): diabetes, stroke, Transient Ischaemic Attack (TIA), hypertension, hyperlipidaemia, Myocardial Infarction (MI), angina, renal failure and renal calculi. Anxiety was ascertained using the Generalised Anxiety Disorder -7 (GAD-7) questionnaire which has a score ranging from 0 to 21. Case definitions were as follows: minimal anxiety 0 to 4, mild 5 to 9, moderate 10 to 14 and severe 15 to 21 (Spitzer, Kroenke et al. 2006). Depression was ascertained using the Patient Health Questionnaire-9 (PHQ-9) which has a score ranging from 0 to 27. Case definitions were as follows: minimal 0 to 4, mild 5 to 9, moderate 10 to 14, moderately severe 15 to 19, severe 20 to 27 (Kroenke, Spitzer et al. 2001). The presence or absence of any

body pain was assessed using a 'yes' or 'no' response option to the question: "During the past month, have you experienced pain affecting any part of the body lasting at least one day?" (Lacey, Lewis et al. 2005).

6.3.3 Socio-demographic characteristics

Age, gender and neighbourhood deprivation (Multiple Deprivation Indices, MDI) were ascertained from general practice records. Relationship status was assessed using a six response options (married, co-habiting, single, widowed, separated or divorced). Ethnicity was also ascertained using six response options (White/ European, Asian, Afro-Caribbean, African, Chinese or other). A 'yes' or 'no' response option was provided for attendance at higher education. Those who attended higher education were asked age (years) at which they left it. Body Mass Index (BMI) was calculated from self-reported height (feet and inches or centimetres) and weight (stones and pounds or kilograms). Alcohol consumption was assessed using six response options (never, special occasions only, 1 to 3 times a month, once or twice a week, 3 to 4 times a week and daily or almost daily).

6.3.4 HRQOL

Generic HRQOL was assessed using the PF-10 and HAQ-DI. Gout-specific HRQOL was assessed using the GIS. The subscales of the GIS as well as the categories and number of items of the HAQ-DI and PF-10 have been described in sections 4.2.4 (impact of gout on quality of life) and 4.2.5 (general health and co-morbidity) in chapter 4 (Study design and methods). All HRQOL questionnaires (GIS, HAQ-DI and PF-10) were measured on a continuous interval scale. The PF-10 is scored as per protocol (White, Wilson et al. 2011) – the 10 items are each rated on a five-point scale each. Raw scores of each question are transformed into a 0 to 100 scale. The HAQ-DI comprises of 20 items in eight categories. Each item is rated on a four-point scale. The highest

score of the sub-category items represent the score of that category. The final score is derived by dividing the sum of the category scores by the number of categories answered (Bruce, Fries 2003a). Each GIS sub-scale could only be scored if at least half of the items of a scale were completed. The Likert scale response for each item within the scale was recoded as per the scoring manual. For each sub-scale the mean of the specified recoded items were calculated. Full scoring instructions for the GIS have been obtained with permission from the authors (Hirsch et al, (Hirsch, Lee et al. 2008)) through personal communication. Scoring of the three HRQOL questionnaires were performed by the study statistician (Sara Muller) and interpretation of the scores is described below in section 6.4.2.

6.4 Analysis

6.4.1 Definition of gout, co-morbid and socio-demographic characteristics by dichotomous or categorical outcomes

Gout, co-morbid and socio-demographic characteristics were considered independent variables. Prior to analysis, all continuous independent variables were transformed into categorical data of two types - nominal variables with binary outcomes (no particular order to the two categories) and ordinal variables (ordered categories of outcome). All ordinal variables along with their categorical outcomes are presented in Table 6-1 below.

6.4.1.1 Gout characteristics

Age (years) at the time of diagnosis of gout was used to calculate disease duration (continuous variable). Disease duration was then categorised into nine-year age bands: 0 to 9, 10 to 19, 20 to 29, 30 to 39 and ≥ 40 years. The dose of allopurinol had multiple response options ranging from 50 mg to 900 mg, dose unknown and any other doses. These were collapsed into 3 categories of

doses: 50 mg to 100 mg, 150 mg to 300 mg and > 300 mg. The cut-off points for each category were decided based on the frequency of responders in each: n= 225 for doses between 50 to 100 mg, n= 361 for doses between 150 to 300 mg and n= 28 for doses between 300 and 900 mg (hence collapsed into one category > 300 mg). One person reported taking allopurinol 150 mg hence this was used as the lowest value (instead of 200 mg) through range 300 mg for the middle category. SUA (continuous variable) was categorised into values ≤ 360 $\mu\text{mol/L}$ and above, based on the target level for urate-lowering treatment (ULT) (Zhang, Doherty et al. 2006b). The 'frequency of attack' categories were left unchanged, as were the following variables with binary outcomes: tophi, a history of oligo or polyarticular attacks, currently having an attack of gout and currently taking allopurinol.

6.4.1.2 Co-morbid characteristics

Scores of anxiety (GAD-7) and depression (PHQ-9) were categorised according to previously validated cut-offs for severity groups. For the GAD-7 the scores were categorised into severity groups as follows: minimal 0 to 4, mild 5 to 9, moderate 10 to 14 and severe 15 to 21 (Spitzer, Kroenke et al. 2006). For the PHQ-9, the scores were categorised into severity groups as follows: minimal 0 to 4, mild 5 to 9, moderate 10 to 14, moderately severe 15 to 19, severe 20 to 27 (Kroenke, Spitzer et al. 2001). Medical co-morbidities (diabetes, stroke, TIA, hypertension, hyperlipidaemia, kidney failure, MI, renal calculi, angina) and body pain were left unchanged as having binary outcomes (presence or absence of variable).

6.4.1.3 Socio-demographic characteristics

According to convention, BMI (continuous variable) was categorised as per the World Health Organisation case definitions (WHO Expert Consultation 2004): underweight (less than or equal to 18.4), normal (18.5 to 24.9), overweight (25 to 29.9) and obese (≥ 30). Based on understanding the difference between HRQOL in those who lived with another person and those who lived alone, the six response options of relationship status were collapsed into 2 categories: married or co-habiting and others (to include separated, divorced, widowed and single). To ascertain the difference in HRQOL between Caucasians (the predominant population in this area¹⁵) and non-Caucasians, the six response options of ethnicity were collapsed into 2 categories: Caucasian and non-Caucasian (to include Asian, afro-Caribbean, African, Chinese and other). Assuming that most people take the 'advanced level' examinations aged 18 and an average university (higher education) course is three years long, the age at which higher education was left (continuous variable) was dichotomised into under 21 years or 21 years and over. Age (continuous variable) was categorised into <40, 19-year age bands from 40 to 79 and ≥ 80 years. Dichotomous outcomes of gender and further education as well as the six categories (frequency) of alcohol consumption were left unchanged.

¹⁵ <http://www.nomisweb.co.uk/census/2011/KS201EW/view/2013265925?cols=measures>

Table 6-1: Classification of gout, co-morbid and socio-demographic variables into ordinal data

Ordinal	Categories
Gout characteristics	
Allopurinol dose (mg)	50 – 100
	150 – 300
	>300
Disease duration (years)	0 to 9
	10 to 19
	20 to 29
	30 to 39
	Equal to or greater than 40
Number of gout attacks over last 12 months	0
	1
	2
	3
	4
	≥5
Frequency of alcohol intake	Daily
	3-4 time a week
	1-2 times a week
	1-3 times a month
	Special occasions
	Never
Socio-demographic characteristics	
MDI neighbourhood deprivation	Most deprived
	Second most deprived
	Mid -deprived
	Second least deprived
	Least deprived
BMI (Kg/m ²)	Less than or equal to 18.4
	18.5 to 24.9
	25 to 29.9
	Greater than or equal to 30
Age (years)	Less than 40
	40 to 59
	60 to 79
	Greater than or equal to 80
Co-morbid characteristics	
Anxiety level	None
	Mild
	Moderate
	Severe
Depression level	None/minimal
	Mild
	Moderate
	Moderately severe
	Severe

6.4.2 Interpretation of the scores of HRQOL

Higher scores represent better HRQOL in the PF-10. There are no pre-defined cut-offs for poor HRQOL in the PF 10 but scores can be compared to UK normative scores (Jenkinson, Coulter et al. 1993). As per consensus, for the HAQ-DI, a score of 0 to 1 represents no or mild disability, >1 to 2 indicated moderate and >2 to 3 severe disability (Krishnan, Tugwell et al. 2004). The Gout Impact Scale (GIS) comprises of five scales – higher scores (range 0 to 100) represent worse HRQOL or greater impact of gout (Hirsch, Lee et al. 2008).

6.4.2.1 Mean scores of HRQOL grouped by responders' characteristics

Mean (standard deviation) HRQOL scores (for PF-10, HAQ-DI and GIS) were stratified by gout, co-morbid and socio-demographic characteristics. Differences between the mean scores were calculated using Analysis of Variance (ANOVA) for ordinal variables with multiple (categorical) outcomes. ANOVA compares the variation between groups to that within groups. It assumes that data are normally distributed with equal variances (homoscedasticity) (Bland 2000). All categorical independent variables were tested for skewness and considered to be normally distributed if the absolute value was ≤ 2 (Hoyle 1995). For all variables of interest, the absolute skewness was < 2 except anxiety and depression (2.16 for both). However as skewness was close to the cut-off and sample size was large ($n > 1000$) for both anxiety and depression, these two variables were considered to be normally distributed for the purpose of ANOVA. The independent samples t-test was used to assess the difference between the mean HRQOL for nominal variables with binary outcomes. Assumptions of normality and equal variance of the study population for the t-test (Jordan, Ong et al. 1998) were considered true given the large sample size ($n > 1000$). All calculations were performed using SPSS 21.

6.5 Results

The overall HRQOL mean (SD) scores are presented below in Table 6-2. The overall mean (SD) HAQ-DI is 0.51 (0.71) and PF-10 75.86 (2.12). Gout-specific HRQOL scores measured using the GIS range from 33.46 for unmet treatment need to 48.65 for concern overall.

Table 6-2: Mean HRQOL scores of survey responders

	Mean (SD)
PF-10¹⁶	75.86 (26.12)
HAQ-DI¹⁷	0.51 (0.71)
GIS¹⁸ CO	48.65 (28.33)
GIS MSE	40.45 (26.33)
GIS UTN	33.46 (20.57)
GIS WBDA	45.19 (26.41)
GIS CDA	40.13 (24.35)

¹⁶ Higher PF 10 scores indicate better health (range 0-100)

¹⁷ Higher HAQ-DI scores indicate greater functional limitations (range 0-3). Median 0.13 and IQR 0 to 0.86

¹⁸ Higher GIS sub-scale scores indicate worse health or greater impact of gout (range 0-100)

6.5.1 Mean HRQOL scores grouped by independent variables

HRQOL scores are presented for independent (potential explanatory) variables. All analyses (in this chapter) to test for differences in HRQOL stratified by the independent variables are unadjusted.

6.5.1.1 Gout variables with binary outcomes

Specific HRQOL scores stratified by gout characteristics with binary outcomes are listed in Table 6-3 below. Using the independent samples t-test, a statistically significant difference between the mean scores of two groups were represented by a confidence interval that excluded 0 and p value < 0.05.

Current gout attack

Participants who reported having an acute attack of gout at the time of questionnaire completion reported greater limitation of their physical functioning as evident by the lower mean score in the PF-10 (mean difference 14.3, 95% CI 8.53, 20.07) and higher mean score in the HAQ-DI (mean difference 0.41, 95% CI 0.25, 0.56). Greater impact of gout was seen across all five sub-scales of the GIS in the presence of an acute attack of gout (mean differences and 95% CI presented in Table 6-3).

Oligo or polyarticular attacks

Those with a history of oligo or polyarticular attack of gout had lower mean score in the PF-10 (mean difference 8.96, 95% CI 5.53, 12.40) and higher mean score in the HAQ-DI (mean difference 0.28, 95% CI 0.20, 0.37), indicating greater limitation or disability compared to those who reported only ever having monoarticular joint involvement. The impact of a history of oligo or polyarticular attacks was greater across all sub-scales of the GIS except unmet treatment need.

Treatment with allopurinol

Those on allopurinol reported lower unmet treatment needs (mean difference 11.56, 95% CI 9.10, 14.01). However, these participants also had greater disability (higher HAQ-DI, mean difference 0.12, 95% CI 0.03, 0.20,) and greater impact on well being during an attack (mean difference 5.08, 95% CI 1.92, 8.25). Mean differences between the scores of those taking allopurinol and those not taking allopurinol were not statistically significant in the PF-10 and other sub-scales of the GIS.

Tophaceous gout

There were no statistically significant differences between the mean scores in the presence or absence of tophi across the gout-specific and generic questionnaires. Only 25 (2.3%) responders who consented for medical record review had a documented presence of tophi.

Serum Uric Acid levels

In the presence of a SUA above the treatment target ($\text{SUA} > 360 \mu\text{mol/L}$) GIS concern for gout overall and unmet treatment need were significantly greater. There were no statistically significant differences between the mean HRQOL scores of those with SUA above and below the treatment target in the PF-10 and HAQ-DI.

Table 6-3: HRQOL scores of participants grouped according to gout-specific characteristics¹⁹ (dichotomous)

HRQOL scores	Currently having an attack of gout		History of O/P attacks		On allopurinol		Tophi		SUA ≤ 360	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Mean (SD) PF-10 ²⁰	63.51	77.81	70.87	79.83	75.70	77.25	68.96	76.57	75.55	76.95
	(27.21)	(25.16)	(26.41)	(24.62)	(25.15)	(26.40)	(30.80)	(25.46)	(24.44)	(25.70)
Mean difference (95% CI)	-14.30 <i>(-20.07, -8.53)</i>		-8.96 <i>(-12.40, -5.53)</i>		-1.55 (-4.93, 1.83)		7.61 (-6.13, 21.36)		-1.39 (-7.23, 4.44)	
Mean (SD) HAQ-DI ²¹	0.86	0.46	0.68	0.39	0.55	0.44	0.79	0.49	0.54	0.50
	(0.82)	(0.68)	(0.78)	(0.64)	(0.74)	(0.67)	(0.91)	(0.70)	(0.71)	(0.70)
Mean difference (95% CI)	0.41 <i>(0.25, 0.56)</i>		0.28 <i>(0.20, 0.37)</i>		0.12 <i>(0.03, 0.20)</i>		-0.30 (-0.68, 0.083)		0.04 (-0.11, 0.20)	

¹⁹ Statistical significance set at p < 0.05. **Mean differences (95% CI) in bold and italics are statistically significant**

²⁰ Higher PF 10 scores indicate better health (range 0-100)

²¹ Higher HAQ-DI scores indicate greater functional limitations (range 0-3)

HRQOL scores	Currently having an attack of gout		History of O/P attacks		On allopurinol		Tophi		SUA ≤ 360	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Mean (SD) GIS ²² CO	71.89 (22.40)	45.65 (27.63)	58.36 (26.64)	42.44 (27.61)	47.13 (28.90)	49.73 (27.59)	46.25 (30.62)	49.25 (28.18)	46.31 (27.25)	55.64 (27.13)
Mean difference (95% CI)	26.24 (21.94, 30.55)		15.93 (12.64, 19.21)		-2.60 (-5.99, 0.78)		3.00 (-9.75, 15.74)		-9.33 (-15.33, -3.34)	
Mean (SD) GIS MSE	56.04 (24.25)	38.23 (25.94)	48.52 (26.61)	34.72 (24.68)	40.00 (25.78)	39.81 (27.09)	46.88 (32.81)	40.73 (25.93)	41.51 (29.96)	43.88 (25.70)
Mean difference (95% CI)	17.82 (13.14, 22.49)		13.80 (10.63, 16.96)		0.19 (-3.02, 3.41)		-6.15 (-20.08, 7.79)		-2.37 (-8.75, 4.01)	
Mean (SD) GIS UTN	50.28 (21.63)	31.39 (19.61)	34.78 (21.53)	32.61 (20.05)	28.62 (19.54)	40.17 (20.36)	38.54 (20.97)	33.07 (20.30)	31.55 (22.92)	36.96 (19.75)

²² Higher GIS sub-scale scores indicate worse health or greater impact of gout (range 0-100)

HRQOL scores	Currently having an attack of gout		History of O/P attacks		On allopurinol		Tophi		SUA ≤ 360	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Mean difference (95% CI)	18.89 (14.77, 23.00)		2.17 (-0.42, 4.76)		-11.56 (-14.01, -9.10)		-5.47 (-14.41, 3.46)		-5.41 (-10.36, -0.46)	
Mean (SD) GIS WBDA	51.22 (24.60)	44.25 (26.56)	53.64 (25.32)	39.48 (25.65)	47.07 (26.35)	41.99 (26.40)	41.32 (24.74)	45.99 (26.13)	42.92 (27.41)	47.00 (26.02)
Mean difference (95% CI)	6.97 (2.36, 11.58)		14.16 (11.07, 17.25)		5.08 (1.92, 8.25)		4.67 (-5.89, 15.22)		-4.08 (-10.04, 1.88)	
Mean (SD) GIS CDA	50.30 (25.81)	38.59 (23.84)	46.62 (24.81)	35.53 (23.03)	40.82 (24.78)	38.40 (23.79)	40.25 (24.35)	40.69 (24.12)	38.46 (24.35)	42.48 (24.73)
Mean difference (95% CI)	11.71 (6.94, 16.48)		11.08 (8.14, 14.03)		2.41 (-0.51, 5.33)		0.44 (-9.71, 10.58)		-4.02 (-9.38, 1.35)	

Abbreviations: O/P: Oligo or Polyarticular; HAQ-DI: Health Assessment Questionnaire Disability Index; PF-10: Physical Function 10; GIS: Gout Impact Scale; CO: Concern Overall; MSE: Medication Side-effects; UTN: Unmet Treatment Needs; WBDA: Wellbeing during attack; CDA: Concern During Attack; SD: Standard Deviation; CI: Confidence Interval

6.5.1.2 Gout variables with categorical outcomes

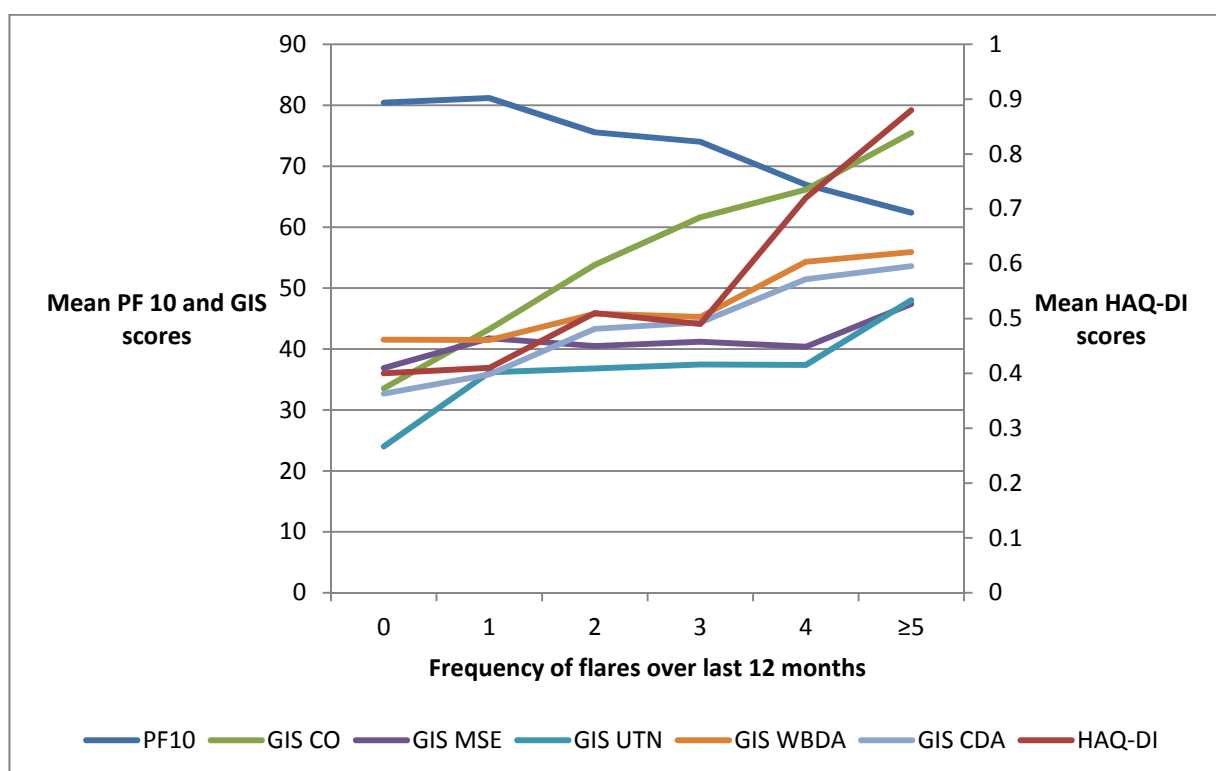
HRQOL scores grouped by gout variables with categorical outcomes are presented in Table 6-4.

Differences between HRQOL of various outcome groups are tested using ANOVA and statistical significance of differences between the mean scores of groups was set a $p < 0.05$. HRQOL scores are represented visually in Figure 7 to Figure 9.

Frequency of gout attacks over the last 12 months

The impact of gout across all five sub-scales of the GIS was greater as the frequency of attacks over the preceding 12 months increased (see Figure 7). There was a marked increase in disability (HAQ-DI) and perceived functional limitation (PF-10), as well as the impact of gout (GIS) as the frequency of attacks increased beyond three in the last year. The differences in HRQOL measured by all instruments were statistically significant ($p < 0.01$ for PF-10, HAQ-DI and GIS, see Table 6-4).

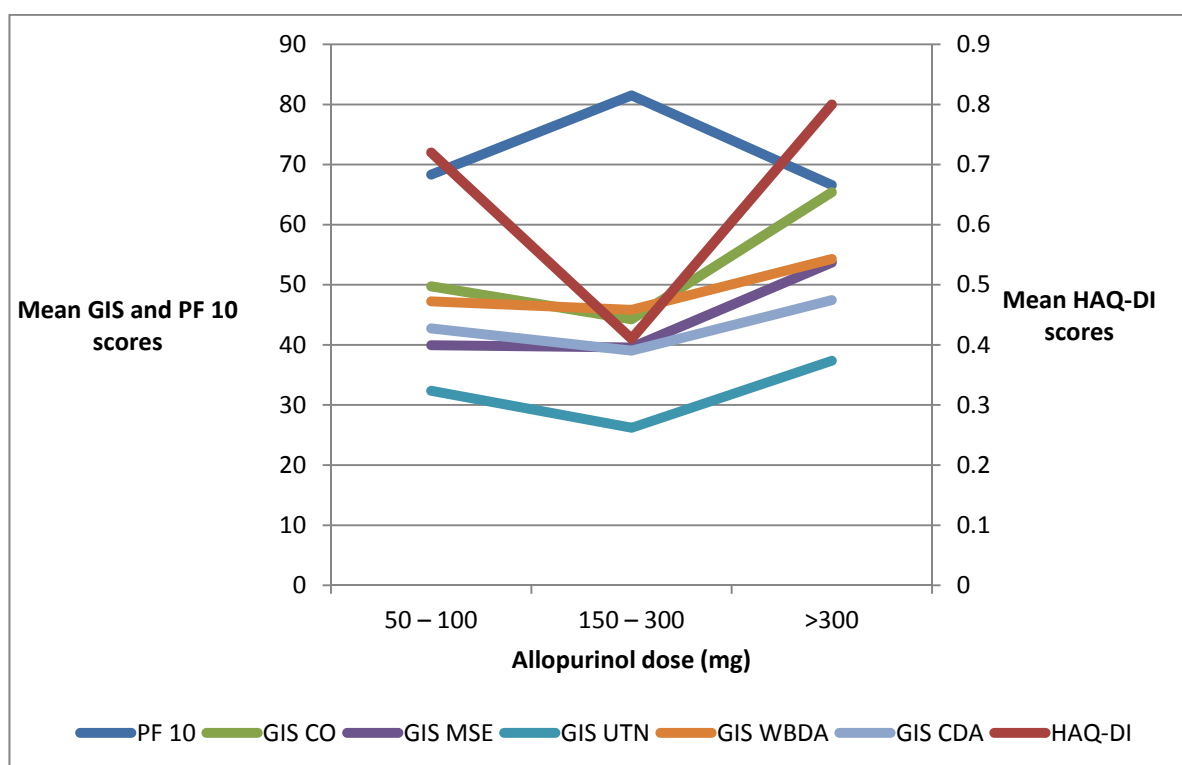
Figure 7: HRQOL scores grouped by frequency of attacks



Dose of allopurinol

The dose of allopurinol and HRQOL in the HAQ-DI exhibited an almost U shaped relationship – at the lower (50 mg to 100 mg) and higher doses (> 300 mg) disability was greater compared to those on 150 mg to 300 mg of allopurinol (see Figure 8). Similarly functional limitation was lowest amongst those on 150 mg to 300 mg allopurinol compared to the other dose categories ($p < 0.01$ for both HAQ-DI and PF-10). The impact of gout was greater (higher GIS concern overall, unmet treatment need) in those taking allopurinol > 300 mg. Concerns about greater medication side-effects were seen in those taking allopurinol > 300 mg ($p 0.023$).

Figure 8: HRQOL scores grouped by allopurinol dose (mg) collapsed into 3 categories



Disease duration (years)

Functional limitation in the PF-10 was greatest in those with longest disease duration (differences between the mean PF 10 scores statistically significant, $p = 0.01$). The GIS concern for gout and

unmet treatment needs however were lesser with increasing duration of disease ($p = 0.006$ for concern overall, $p < 0.01$ for unmet treatment need). Although the impact of gout was lesser in the other sub-scales of the GIS (medication side-effects, well-being and concern during attack), the differences between the mean scores of participants were not statistically significant ($p > 0.05$). Similarly, although disability (HAQ-DI) was greatest in those with longest disease duration, particularly > 30 years (see Figure 9), the difference between the mean HAQ-DI scores was not statistically significant ($p = 0.32$).

Figure 9: HRQOL scores grouped by disease duration

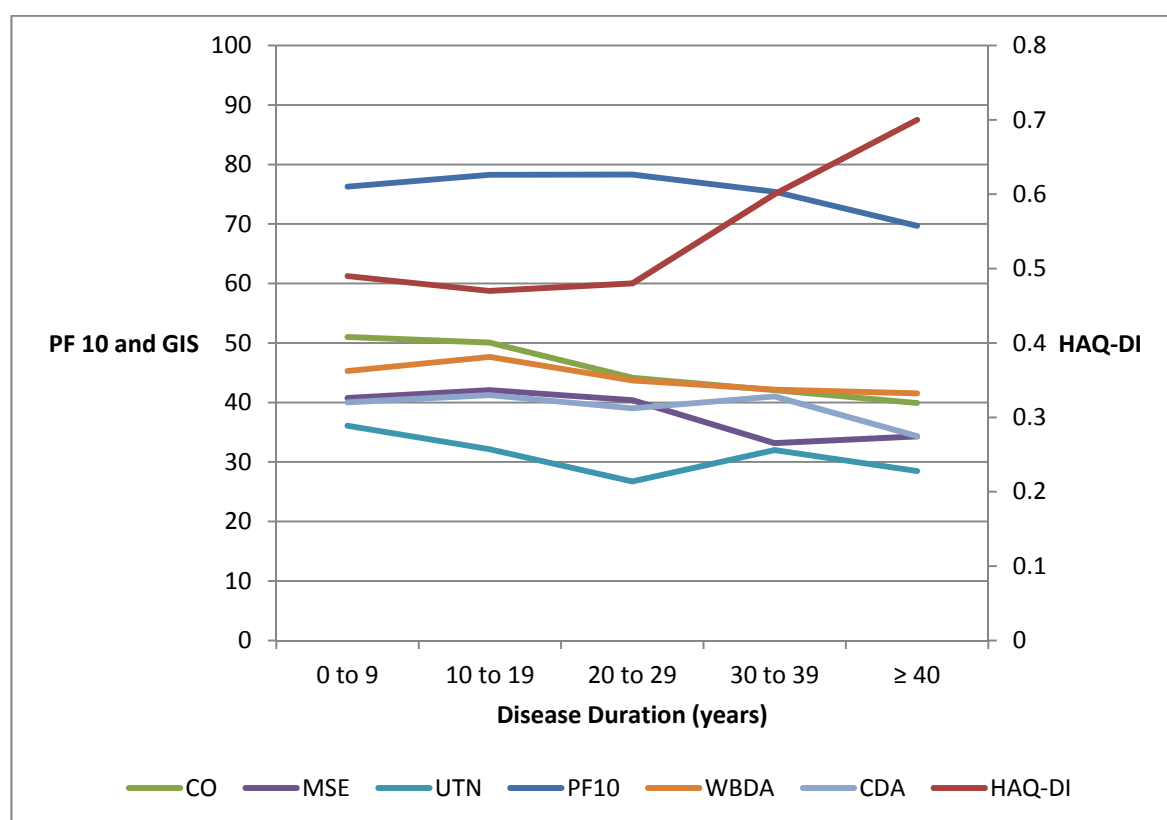


Table 6-4: HRQOL in participants grouped by gout-specific characteristics with ordinal outcomes

		Mean PF 10	Mean HAQ-DI	Mean CO	Mean MSE	Mean UTN	Mean WBDA	Mean CDA
		(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
Allopurinol dose (mg)	50 to 100	68.33 (64.21, 72.46)	0.72 (0.60, 0.83)	49.75 (45.90, 53.60)	39.94 (36.39, 43.50)	32.36 (29.77, 34.96)	47.23 (43.60, 50.86)	42.73 (39.33, 46.13)
	150 to 300	81.51 (78.94, 84.07)	0.41 (0.35, 0.48)	44.27 (41.31, 47.23)	39.57 (36.92, 42.22)	26.21 (24.23, 28.20)	45.82 (43.15, 48.50)	39.04 (36.52, 41.56)
	>300	66.60 (53.62, 79.58)	0.80 (0.47, 1.14)	65.40 (55.24, 75.57)	53.70 (42.92, 64.49)	37.35 (30.32, 44.38)	54.29 (44.10, 64.47)	47.45 (36.63, 58.28)
P value		< 0.01	< 0.01	< 0.01	0.023	< 0.01	0.24	0.080
Disease duration (years)	0 to 9	76.28 (74.00, 78.57)	0.49 (0.44, 0.55)	50.99 (48.68, 53.30)	40.75 (38.56, 42.93)	36.08 (34.34, 37.82)	45.30 (43.13, 47.47)	40.02 (37.99, 42.05)
	10 to 19	78.26 (74.70, 81.82)	0.47 (0.39, 0.56)	50.04 (46.36, 53.73)	42.05 (38.57, 45.53)	32.14 (29.52, 34.77)	47.66 (44.30, 51.02)	41.24 (38.05, 44.43)
	20 to 29	78.28 (73.52, 83.05)	0.48 (0.36, 0.61)	44.15 (39.73, 48.58)	40.38 (36.29, 44.47)	26.74 (23.54, 29.93)	43.70 (39.59, 47.82)	39.01 (35.26, 42.76)
	30 to 39	75.42 (68.34, 82.50)	0.60 (0.42, 0.78)	42.06 (35.30, 48.81)	33.15 (27.35, 38.95)	32.00 (27.30, 36.71)	42.17 (35.53, 48.80)	41.00 (35.71, 46.29)

[illegible]

	Mean PF 10	Mean HAQ-DI	Mean CO	Mean MSE	Mean UTN	Mean WBDA	Mean CDA
	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)

Abbreviations: mg: Milligrams; CI: Confidence Interval; PF-10: Physical Function-10; HAQ-DI: Health Assessment Questionnaire Disability Index; GIS CO: Gout Impact Scale Concern Overall; MSE: Medication Side-effects; UTN: Unmet Treatment Need; WBDA: Wellbeing During Attack; CDA: Concern During Attack

6.5.1.3 Co-morbid characteristics

The differences between mean HRQOL scores (95% CI) stratified by co-morbidities which have a dichotomous response option (yes/no) are presented in Table 6-5 and Table 6-6. HRQOL scores stratified by anxiety and depression, both of which have outcomes ranging from none to severe (categorical) are presented in Table 6-7. Functional limitations (PF-10) and disability (HAQ-DI) were greater in the presence of diabetes and hypertension (compared to the absence of diabetes and hypertension). Lesser concerns about medication side-effects (GIS) were reported in the presence of diabetes compared to the absence of diabetes. Similarly those with hypertension reported lower concern overall when compared to those without hypertension. The co-existence of hyperlipidaemia with gout was associated with greater disability (HAQ-DI) but not with functional limitation (PF-10) or worse HRQOL in the GIS.

Greater disability (HAQ-DI), functional limitation (PF-10) and GIS concern overall were seen in those with renal failure compared with those without renal failure. Having renal calculi (compared to not having renal calculi) was associated with significantly greater concerns about medication side effects in the GIS.

Table 6-5: HRQOL scores stratified by diabetes, hypertension, hyperlipidaemia and renal disease²³

HRQOL scores	Diabetes		Hypertension		Hyperlipidaemia		Kidney failure		Renal calculi	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Mean (SD) PF-10	66.44 (26.83)	77.87 (25.55)	72.67 (25.82)	80.79 (25.83)	74.12 (25.43)	77.17 (26.54)	57.48 (25.47)	76.73 (25.85)	77.36 (24.68)	75.82 (26.22)
Mean difference (95% CI)	11.43 (6.94,15.92)		8.13 (4.78, 11.47)		3.05 (-0.28, 6.38)		19.25 (11.05, 27.44)		-1.54 (-8.30, 5.22)	
Mean (SD) HAQ-DI	0.80 (0.86)	0.45 (0.66)	0.59 (0.75)	0.38 (0.62)	0.56 (0.74)	0.47 (0.69)	1.04 (0.86)	0.48 (0.69)	0.64 (0.72)	0.50 (0.71)
Mean difference (95% CI)	-0.35 (-0.48, -0.22)		-0.21 (-0.29, -0.13)		-0.09 (-0.18, -0.01)		-0.56 (-0.79, -0.32)		-0.15 (-0.31, 0.02)	
Mean (SD) GIS CO	46.03 (29.04)	49.24 (28.14)	47.20 (28.16)	51.12 (28.44)	48.40 (28.65)	48.89 (28.08)	58.73 (24.19)	48.19 (28.42)	53.60 (29.85)	48.32 (28.18)
Mean difference (95% CI)	3.21 (-1.22,7.63)		3.92 (0.53, 7.31)		0.49 (-2.84, 3.82)		-10.54 (-17.40, -3.67)		-5.28 (-12.25, 1.70)	
Mean (SD) GIS MSE	36.93 (27.19)	41.17 (26.10)	40.03 (26.92)	41.12 (25.32)	40.48 (27.04)	40.41 (25.80)	45.45 (25.61)	40.18 (26.35)	47.76 (26.01)	39.89 (26.28)
Mean difference (95% CI)	4.25 (0.07,8.43)		1.09 (-2.04, 4.23)		-0.07(-3.20, 3.06)		-5.28 (-12.37, 1.82)		-7.86 (-13.93, -1.79)	

²³ Statistical significance set at p < 0.05. **Mean difference (95% CI) in bold and italics are statistically significant**

HRQOL scores	Diabetes		Hypertension		Hyperlipidaemia		Kidney failure		Renal calculi	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Mean (SD) GIS UTN	34.09	33.34	33.32	33.73	33.26	33.63	33.26	33.48	35.88	33.29
	(21.48)	(20.40)	(21.00)	(19.90)	(21.63)	(19.78)	(20.56)	(20.60)	(20.88)	(20.56)
Mean difference (95% CI)	-0.75	(-4.08, 2.57)	0.41	(-2.07, 2.89)	0.36	(-2.12, 2.84)	0.22	(-5.47, 5.91)	-2.59	(-7.49, 2.31)
Mean (SD) GIS WBDA	44.69	45.26	44.54	46.17	45.03	45.25	50.08	44.92	44.16	45.23
	(28.61)	(25.95)	(26.20)	(26.79)	(26.34)	(26.50)	(25.58)	(26.45)	(26.12)	(26.46)
Mean difference (95% CI)	0.57	(-3.75,4.88)	1.63	(-1.54, 4.80)	0.22	(-2.87, 3.31)	-5.16	(-12.31, 1.99)	1.08	(-4.94, 7.10)
Mean (SD) GIS CDA	40.26	40.11	40.13	40.15	40.65	39.75	45.72	39.86	44.56	39.82
	(26.96)	(23.73)	(24.39)	(24.22)	(24.55)	(24.15)	(25.22)	(24.25)	(24.13)	(24.31)
Mean difference (95% CI)	-0.15	(-4.20, 3.90)	0.01	(-2.91, 2.93)	-0.90	(-3.77, 1.96)	-5.86	(-12.89,1.17)	-4.75	(-10.41, 0.92)
Abbreviations: HRQOL: Health Related Quality of Life; SD: Standard Deviation; CI: Confidence Interval; HAQ-DI: Health Assessment Questionnaire Disability Index; PF-10: Physical Function 10; GIS: Gout Impact Scale; CO: Concern Overall; MSE: Medication Side Effects; UTN: Unmet Treatment Need; WBDA: Wellbeing During Attack; CDA: Concern During Attack										

Greater functional limitation (PF-10) and disability (HAQ-DI) were seen in those with a previous stroke compared to those who had not had stroke, but had no effect on HRQOL in the GIS. Similarly having MI or angina (ischaemic heart disease, IHD) was associated with greater disability (HAQ-DI) and functional limitation (PF- 10) compared to not having IHD but did not affect HRQOL in the GIS. In contrast, TIA had no effect on HRQOL in the generic questionnaires but those with TIA had lower GIS concern overall and concerns about well-being during an attack compared to those who had never had a TIA. The presence of any body pain was associated with worse functional limitation (PF-10), disability (HAQ-DI) and greater impact of gout in all sub-scales of the GIS compared to not having any body pain. The difference between mean HRQOL scores (95% CI) in the presence or absence of body pain were statistically significant for all GIS sub-scales (see Table 6-6).

Table 6-6: HRQOL scores in participants grouped by cardiovascular, cerebrovascular and body pain co-morbidity²⁴

	Stroke		TIA		MI		Angina		Body pain	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Mean (SD) PF-10	58.47 (26.13)	76.43 (25.95)	75.68 (25.17)	75.92 (26.18)	71.12 (26.61)	88.69 (17.27)	64.88 (26.26)	77.06 (25.85)	60.82 (26.99)	77.90 (25.35)
Mean difference (95% CI)	17.97 (7.71, 28.22)		0.24 (-7.33, 7.81)		12.18 (6.45, 17.91)		17.08 (11.76, 22.41)		-17.57 (-20.66, -14.48)	
Mean (SD) HAQ-DI	1.02 (0.88)	0.49 (0.70)	0.48 (0.65)	0.51 (0.72)	0.65 (0.77)	0.20 (0.43)	0.78 (0.77)	0.48 (0.70)	0.87 (0.84)	0.46 (0.68)
Mean difference (95% CI)	-0.53 (-0.83, -0.23)		0.03 (-0.14, 0.20)		-0.30 (-0.45, -0.15)		-0.42 (-0.56, -0.27)		0.45 (0.37, 0.53)	
Mean (SD) GIS CO	45.89 (26.08)	48.77 (28.39)	40.63 (27.39)	49.14 (28.31)	53.46 (27.45)	37.50 (27.01)	46.05 (27.21)	48.97 (28.43)	53.46 (27.45)	37.50 (27.01)
Mean difference (95% CI)	2.87 (-6.23, 11.97)		8.51 (1.37, 15.66)		2.92 (-2.42, 8.25)		1.49 (-3.51, 6.50)		15.96 (12.26, 19.65)	
Mean (SD) GIS MSE	35.66 (29.54)	40.59 (26.22)	35.66 (26.99)	40.71 (26.27)	43.94 (26.25)	31.81 (24.74)	40.68 (26.49)	40.41 (26.32)	43.94 (26.25)	31.81 (24.74)

²⁴ Statistical significance set at p < 0.05. **Mean difference (95% CI) in bold and italics are statistically significant**

	Stroke		TIA		MI		Angina		Body pain	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Mean difference (95% CI)	4.92 (-5.49, 15.34)		5.05 (-2.03, 12.14)		-0.27 (-5.44, 4.90)		0.24 (-4.54, 5.02)		12.13 (8.68, 15.58)	
Mean (SD) GIS UTN	29.41 (19.81)	33.60 (20.61)	29.58 (15.30)	33.69 (20.83)	35.38 (20.75)	28.81 (19.61)	34.38 (22.13)	33.37 (20.42)	35.38 (20.75)	28.81 (19.61)
Mean difference (95% CI)	4.19 (-2.83, 11.20)		4.11 (-0.03, 8.25)		-1.02 (-5.37, 3.33)		-1.72 (-5.68, 2.25)		6.57 (3.81, 9.34)	
Mean (SD) GIS WBDA	38.86 (24.95)	45.36 (26.45)	37.90 (24.31)	45.57 (26.49)	49.66 (25.70)	36.82 (25.15)	43.95 (26.16)	45.30 (26.46)	49.66 (25.70)	36.82 (25.15)
Mean difference (95% CI)	6.50 (-2.20, 15.20)		7.67 (1.26, 14.08)		1.34 (-3.73, 6.41)		-1.70 (-6.55, 3.16)		12.84 (9.41, 16.28)	
Mean (SD) GIS CDA	39.89 (22.30)	40.14 (24.39)	36.19 (24.62)	40.36 (24.29)	43.04 (24.50)	32.09 (22.45)	41.61 (25.50)	39.97 (24.19)	43.04 (24.50)	32.09 (22.45)
Mean difference (95% CI)	0.25 (-7.65, 8.16)		4.17 (-2.24, 10.59)		1.64 (-6.59, 3.32)		3.40 (-8.10, 1.30)		10.95 (7.79, 14.10)	

Abbreviations: TIA: Transient Ischaemic Attack; MI: Myocardial Infarction; SD: Standard Deviation; CI: Confidence Interval; PF-10: Physical Function 10; HAQ-DI: Health Assessment Questionnaire Disability Index; GIS: Gout Impact Scale; CO: Concern Overall; MSE: Medication Side Effects; UTN: Unmet Treatment Need; WBDA: Wellbeing During Attack; CDA: Concern During Attack

Greater functional limitation (PF-10), disability (HAQ-DI) and worse HRQOL in the GIS were seen amongst those with severe anxiety or depression compared with those who had milder or no anxiety or depression (see Figure 10 and Figure 11). The differences between the scores stratified by levels of anxiety and depression were statistically significant ($p < 0.01$) for all questionnaires as seen in Table 6-7.

Figure 10: HRQOL scores grouped by levels of anxiety

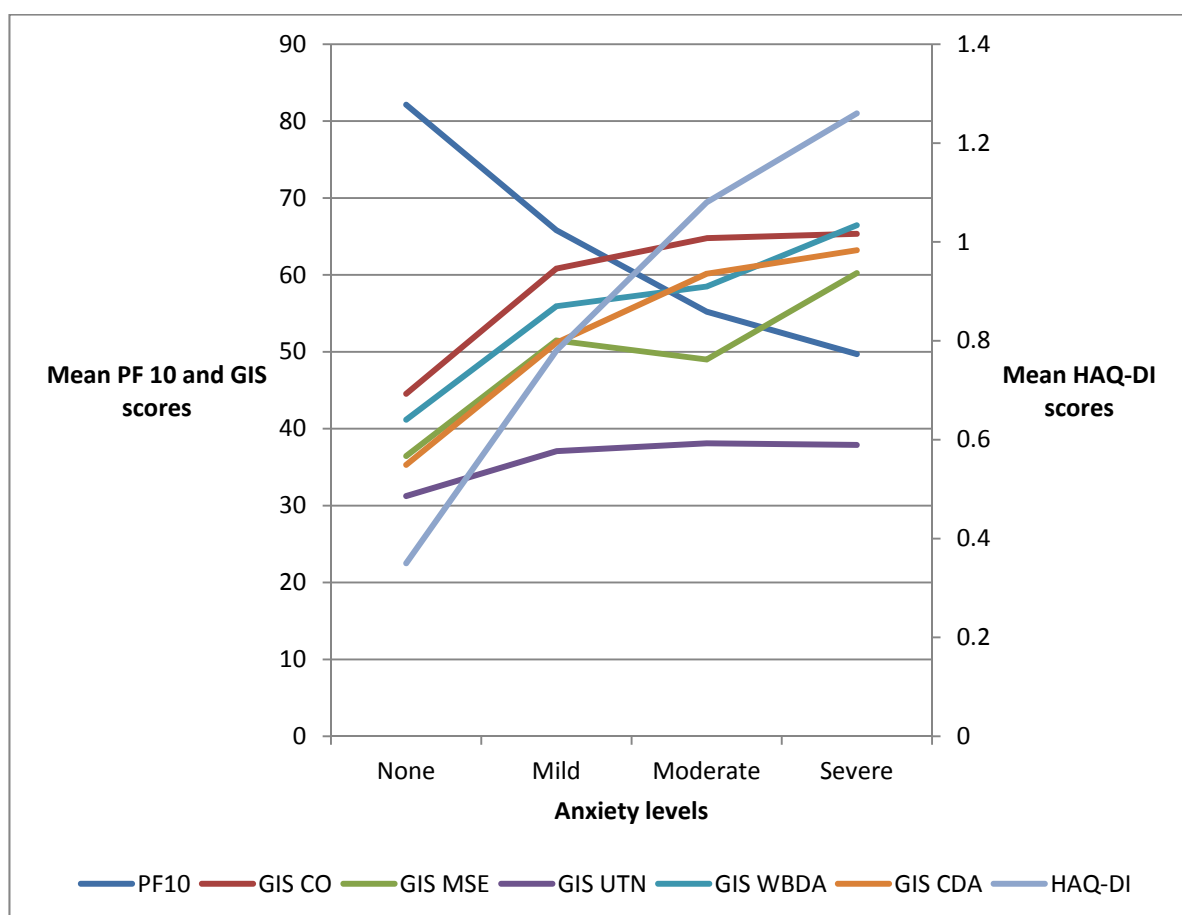


Figure 11: HRQOL scores grouped by levels of depression

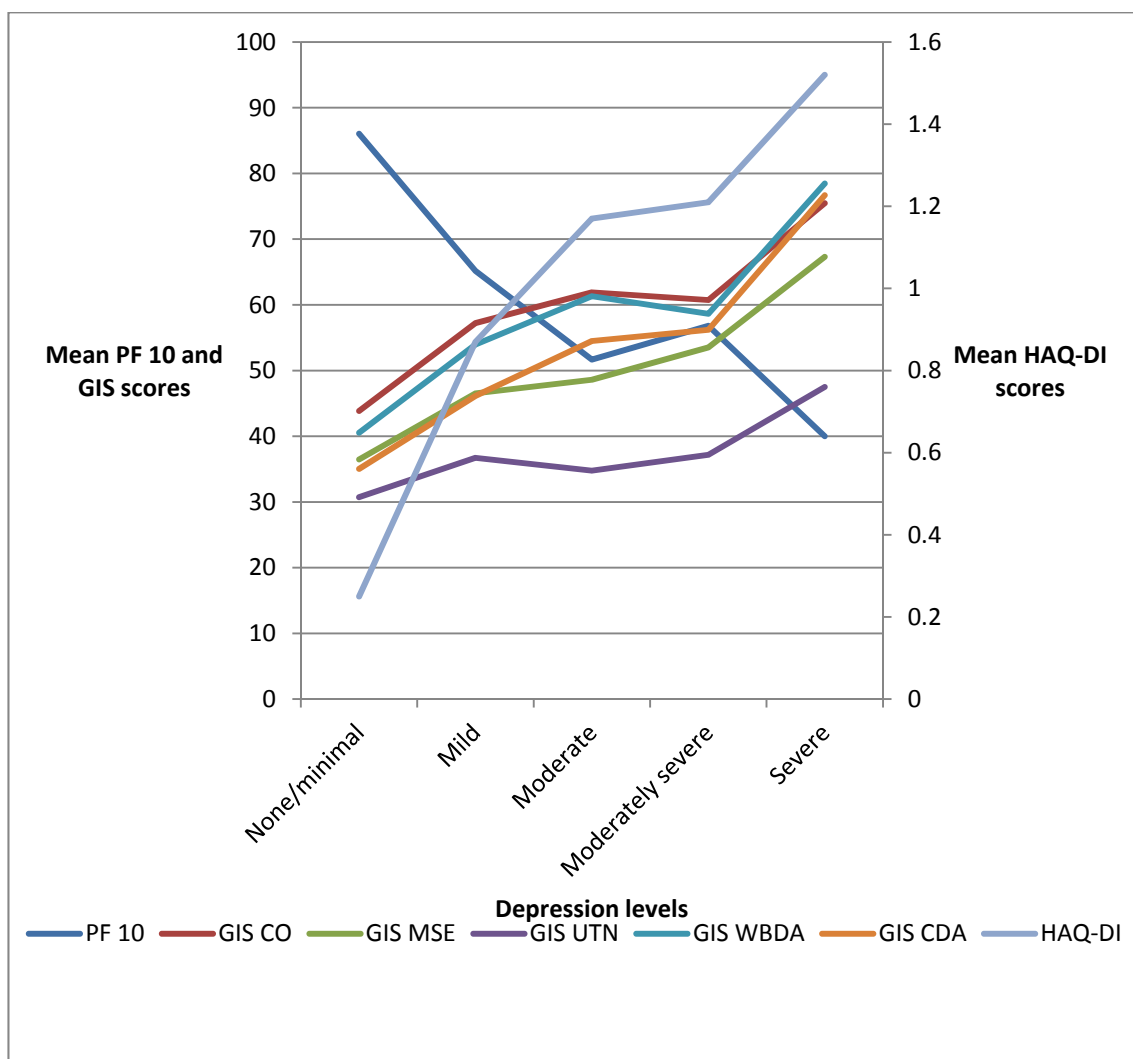


Table 6-7: HRQOL grouped by anxiety and depression

		Mean PF-10	Mean	Mean CO	Mean MSE	Mean UTN	Mean WBDA	Mean CDA
		(95% CI)	HAQ-DI	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
		(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
Anxiety level	None	82.14	0.35	44.54	36.44	31.24	41.18	35.31
		(80.52, 83.77)	(0.31, 0.39)	(42.65, 46.43)	(34.75, 38.12)	(29.88, 32.60)	(39.47, 42.89)	(33.82, 36.81)
	Mild	65.82	0.78	60.81	51.47	37.07	55.93	51.16
		(60.62, 71.01)	(0.64, 0.91)	(56.29, 65.33)	(46.93, 56.01)	(33.55, 40.58)	(51.93, 59.93)	(47.12, 55.19)
	Moderate	55.22	1.08	64.78	48.99	38.10	58.49	60.15
		(47.76, 62.68)	(0.85,1.32)	(58.30, 71.27)	(42.33, 55.65)	(32.51, 43.70)	(51.80, 65.17)	(53.73, 66.56)
	Severe	49.70	1.26	65.34	60.23	37.89	66.45	63.21
		(40.92, 58.47)	(0.95, 1.56)	(56.64, 74.04)	(51.09, 69.36)	(31.14, 44.63)	(57.63, 75.26)	(55.15, 71.27)
P value for ANOVA		< 0.01	< 0.01	<0.01	< 0.01	< 0.01	< 0.01	<0.01
Depression level	None	86.05	0.25	43.84	36.46	30.73	40.53	35.04
		(84.55, 87.55)	(0.22, 0.28)	(41.86, 45.83)	(34.66, 38.27)	(29.31, 32.15)	(38.76, 42.31)	(33.46, 36.62)
	Mild	65.16	0.8	57.22	46.53	36.7	53.95	46.14
		(60.16, 70.15)	(0.73, 1.00)	(52.78, 61.66)	(42.24, 50.82)	(33.19, 40.22)	(50.03, 57.87)	(42.62, 49.65)
	Moderate	51.67	1.1	61.91	48.61	34.77	61.31	54.49
		(45.89, 57.46)	(0.95, 1.39)	(55.32, 68.51)	(41.61, 55.61)	(29.78, 39.75)	(54.78, 67.84)	(47.94, 61.04)

	Mean PF-10 (95% CI)	Mean HAQ-DI (95% CI)	Mean CO (95% CI)	Mean MSE (95% CI)	Mean UTN (95% CI)	Mean WBDA (95% CI)	Mean CDA (95% CI)
Moderately severe	56.80 (47.88, 65.73)	1.21 (0.94, 1.49)	60.74 (50.64, 70.83)	53.53 (43.96, 63.09)	37.18 (30.74, 43.62)	58.64 (50.36, 66.93)	56.20 (47.93, 64.46)
Severe	40.00 (32.60, 47.40)	1.52 (1.09, 1.95)	75.48 (65.93, 85.03)	67.31 (57.61, 77.00)	47.50 (38.51, 56.49)	78.47 (68.37, 88.56)	76.68 (68.91, 84.46)
P value for ANOVA	< 0.01	<0.01	<0.01	< 0.01	< 0.01	< 0.01	< 0.01

Abbreviations: PF-10: Physical Function 10; HAQ-DI: Health Assessment Questionnaire Disability Index; CO: Concern Overall; MSE: Medication Side Effects; UTN: Unmet Treatment Need; WBDA: Wellbeing During Attack; CDA: Concern During Attack; ANOVA: Analysis of Variance; CI: Confidence Interval

6.5.1.4 Socio-demographic characteristics

Female compared to male participants with gout had greater disability (HAQ-DI), functional limitation (PF-10) and greater GIS unmet treatment need. Lesser disability (HAQ-DI), functional limitation (PF-10), lower GIS medication side-effects, unmet treatment need and concern during attack were seen in those who attended further education compared to those who did not. Non-Caucasian ethnicity (compared to Caucasian) was associated with greater GIS concern overall, concern regarding higher medication side-effects, greater unmet treatment needs and higher concern during attacks but was not associated with generic HRQOL. Age < 21 at leaving further education (compared to age > 21 at leaving further education) was associated with worse functional limitation (PF-10) and greater impact of gout in all sub-scales of the GIS except wellbeing during attack (see Table 6-8). Co-habiting with another person or being married was associated with better HRQOL in all sub-scales of the GIS except unmet treatment need, compared to living alone or not being married. It did not however affect generic HRQOL in the PF-10 or HAQ-DI.

Table 6-8: HRQOL scores in participants grouped by socio-demographic factors ²⁵ (dichotomous)

	Gender		Attended further education		Caucasian		Age <21 at leaving further education		Married or co-habiting	
	Male	Female	Yes	No	Yes	No	Yes	No	Yes	No
Mean (SD) PF-10	79.39 (24.86)	57.98 (25.16)	84.19 (21.01)	74.21 (26.60)	76.28 (25.90)	67.30 (25.62)	79.75 (23.25)	88.75 (17.72)	75.41 (26.25)	77.46 (25.69)
Mean difference (95% CI)	21.41 (17.08, 25.74)		9.98 (6.50, 13.46)		8.97 (-2.79, 20.74)		-9.0 (-14.73, -3.27)		-2.05 (-6.00, 1.91)	
Mean (SD) HAQ-DI	0.42 (0.65)	0.96 (0.83)	0.34 (0.57)	0.54 (0.74)	0.50 (0.71)	0.70 (0.68)	0.39 (0.57)	0.30 (0.54)	0.53 (0.73)	0.44 (0.65)
Mean difference (95% CI)	-0.54 (-0.67, -0.41)		-0.21 (-0.29, -0.12)		-0.20 (-0.47, 0.07)		0.09 (-0.05, 0.23)		0.08 (-0.01, 0.18)	
Mean (SD) GIS CO	48.50 (28.49)	49.64 (27.42)	46.39 (28.57)	49.46 (28.22)	48.71 (28.06)	62.42 (30.99)	50.58 (27.44)	43.16 (27.95)	47.74 (28.42)	51.85 (27.84)
Mean difference (95% CI)	-1.14 (-5.52, 3.24)		-3.08 (-7.17, 1.02)		-13.71 (-26.32, -1.09)		7.42 (0.30, 14.53)		-4.10 (-8.01, -0.19)	
Mean (SD) GIS MSE	40.68 (26.13)	39.12 (27.41)	37.34 (25.01)	41.23 (26.48)	40.33 (25.95)	59.13 (30.12)	41.09 (24.71)	34.60 (25.00)	39.61 (26.88)	43.33 (24.14)
Mean difference (95% CI)	1.56 (-2.83, 5.94)		-3.89 (-7.54, -0.23)		-18.81 (-31.06, -6.56)		6.49 (0.08, 12.90)		-3.72 (-7.19, -0.25)	

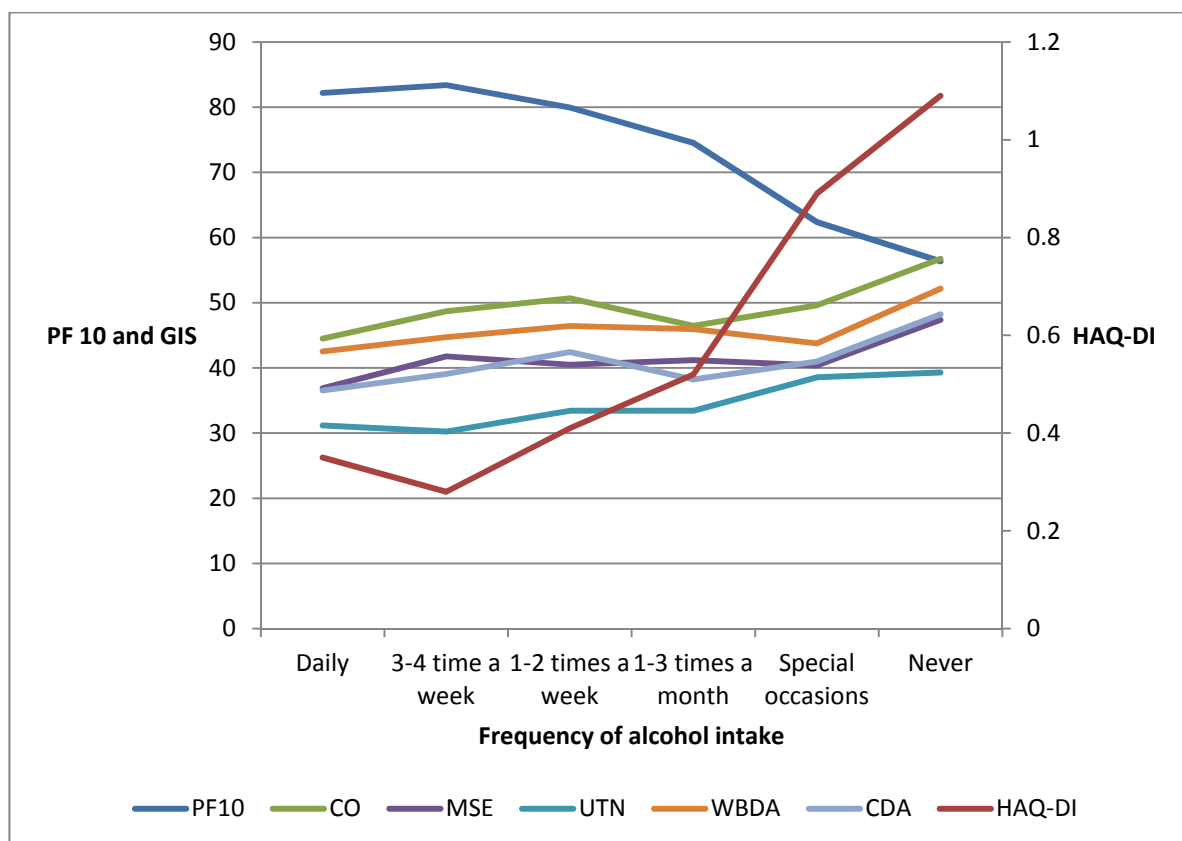
²⁵ Statistical significance set at p < 0.05. **Mean difference (95% CI) in bold and italics are statistically significant**

	Gender		Attended further education		Caucasian		Age <21 at leaving further education		Married or co-habiting	
	Male	Female	Yes	No	Yes	No	Yes	No	Yes	No
Mean (SD)	32.88	36.76	30.35	34.16	33.29	40.87	33.37	27.46	33.47	33.43
GIS UTN	(20.35)	(21.60)	(21.28)	(20.57)	(20.64)	(18.11)	(23.25)	(18.28)	(20.72)	(20.08)
Mean difference	-3.89		-3.81		-7.57		5.91		0.04	
(95% CI)	(-7.41, -0.36)		(-6.90, -0.73)		(-14.98, -0.17)		(0.47, 11.35)		(-2.82, 2.89)	
Mean (SD)	45.78	41.89	43.20	46.07	45.27	56.54	45.75	40.99	43.87	49.84
GIS WBDA	(26.12)	(27.79)	(25.07)	(26.77)	(26.14)	(31.14)	(26.03)	(23.42)	(26.23)	(26.57)
Mean difference	3.88		-2.87		-11.27		4.76		-5.97	
(95% CI)	(-0.49, 8.26)		(-6.51, 0.78)		(-23.44, 0.89)		(-1.58, 11.11)		(-9.67, -2.27)	
Mean (SD)	40.08	40.45	36.46	41.20	40.05	58.33	39.67	33.93	39.24	43.23
GIS CDA	(24.26)	(24.66)	(22.07)	(24.57)	(23.81)	(31.00)	(22.01)	(21.89)	(23.97)	(25.41)
Mean difference	-0.37		-4.74		-18.28		5.74		-3.99	
(95% CI)	(-4.30, 3.56)		(-8.00, -1.49)		(-30.87, -5.69)		(0.09, 11.39)		(-7.50, -0.48)	

Abbreviations: SD: Standard Deviation; CI: Confidence Interval; PF-10: Physical Function 10; HAQ-DI: Health Assessment Questionnaire Disability Index; GIS CO: Gout Impact Scale Concern Overall; MSE: Medication Side Effects; UTN: Unmet Treatment Need; WBDA: Wellbeing During Attack; CDA: Concern During Attack

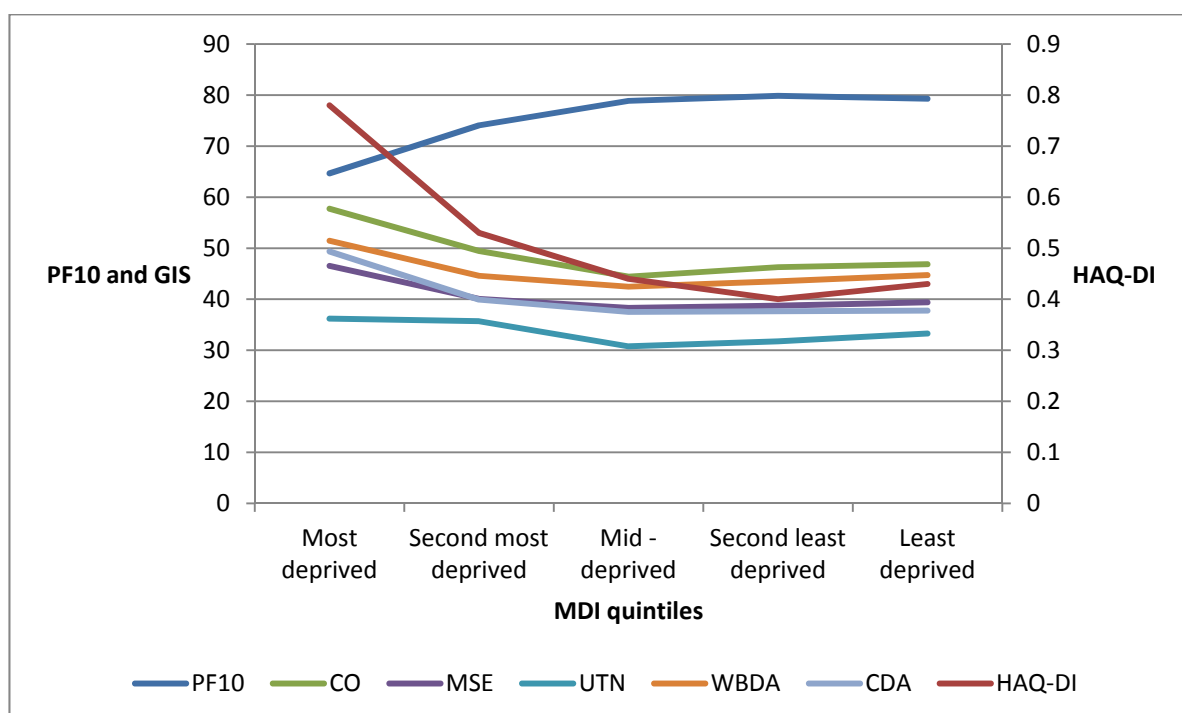
Higher PF-10 scores (better HRQOL) were seen amongst those with daily consumption of alcohol compared to those who refrained from any alcohol consumption at all. The trend however was not linear, with least functional limitation seen in those who consumed alcohol 3 to 4 times a week compared to any other frequency of alcohol intake. Lesser disability (HAQ-DI scores lower) was also seen amongst those with a daily frequency of alcohol consumption compared to no alcohol consumption at all. Similarly, highest GIS CO, MSE, WBDA and CDA scores (worst HRQOL) were seen amongst the group who reported 'never' drinking alcohol and lowest GIS scores (best HRQOL) were associated with drinking alcohol 'daily'. For unmet treatment need, although the highest score (worst HRQOL) was seen in the group who reported the frequency of alcohol consumption as 'never', the lowest (best HRQOL) score were for those who reported drinking alcohol 3 to 4 times a week. The relationship between HRQOL in the GIS and alcohol consumption was less linear than the relationship between HRQOL in the PF-10 and HAQ-DI and alcohol consumption (see Figure 12). The differences between the scores of the groups based on the frequency of alcohol consumption were statistically significant ($p < 0.05$) for all questionnaires (see Table 6-9).

Figure 12: HRQOL scores grouped by frequency of alcohol intake



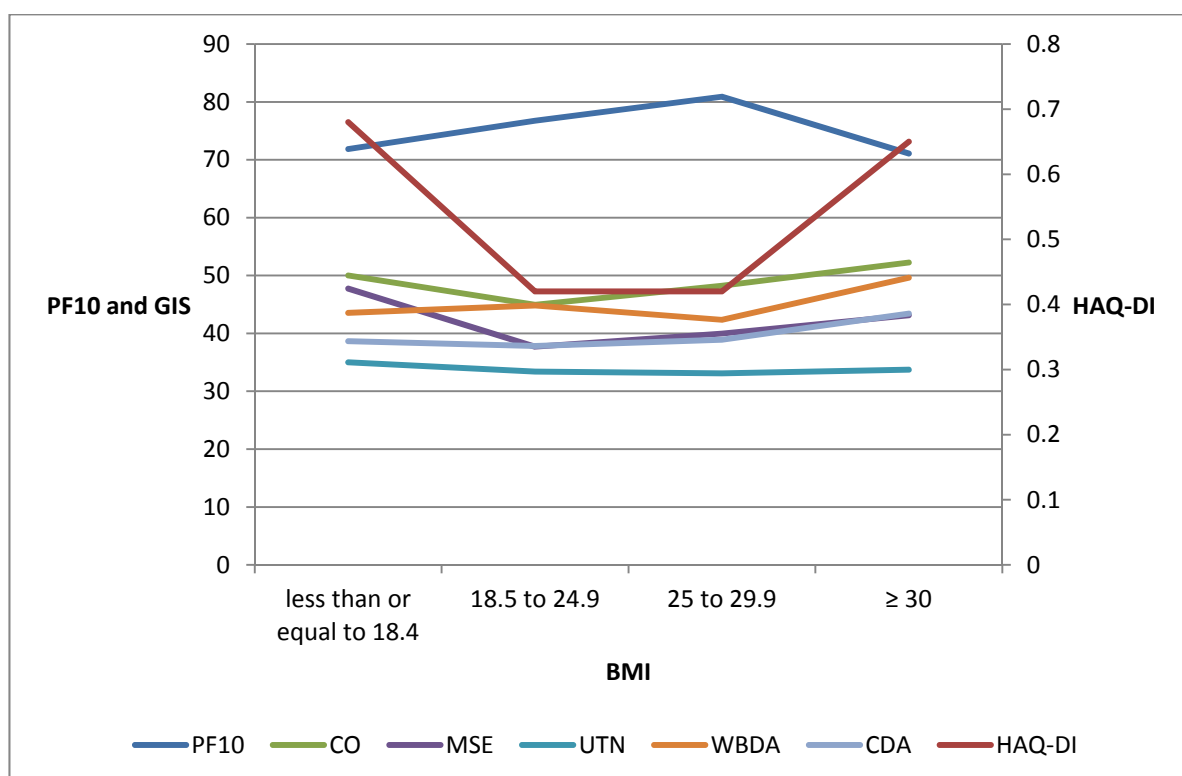
Those living in the most deprived neighbourhood (MDI neighbourhood rankings divided into quintiles) reported greatest functional limitation (PF-10), disability (HAQ-DI) and impact of gout (GIS) (see Figure 13). Although small, the differences between gout-specific and generic HRQOL grouped by MDI quintiles were statistically significant ($p < 0.05$, see Table 6-9).

Figure 13: HRQOL scores grouped by neighbourhood deprivation rankings



Those at extreme ranges of BMI (≤ 18.4 and > 30) had worse functional limitation (PF-10) and disability (HAQ-DI) compared to other BMI groups (see Figure 14). The impact of gout in the GIS (except the treatment sub-scales) was greatest in those who were obese ($\text{BMI} \geq 30$) compared to lower BMI groups. Differences between the scores of the PF-10, HAQ-DI, GIS concern overall and during attack were statistically significant ($p < 0.05$) (see Table 6-9).

Figure 14: HRQOL scores grouped by BMI



Least functional limitation (PF-10) and disability (HAQ-DI) were associated with those aged between 40 to 59 years compared to older age groups (See Figure 15). However better HRQOL in the GIS (except in the unmet treatment need sub-scale) was associated with age above 40 years. This trend was non-linear for concern overall (highest concern overall in the 40 to 59 age group compared to others). The differences between the scores based on age categories are statistically significant ($p < 0.01$) except for the unmet treatment need sub-scale (see Table 6-9).

Figure 15: HRQOL scores grouped by age

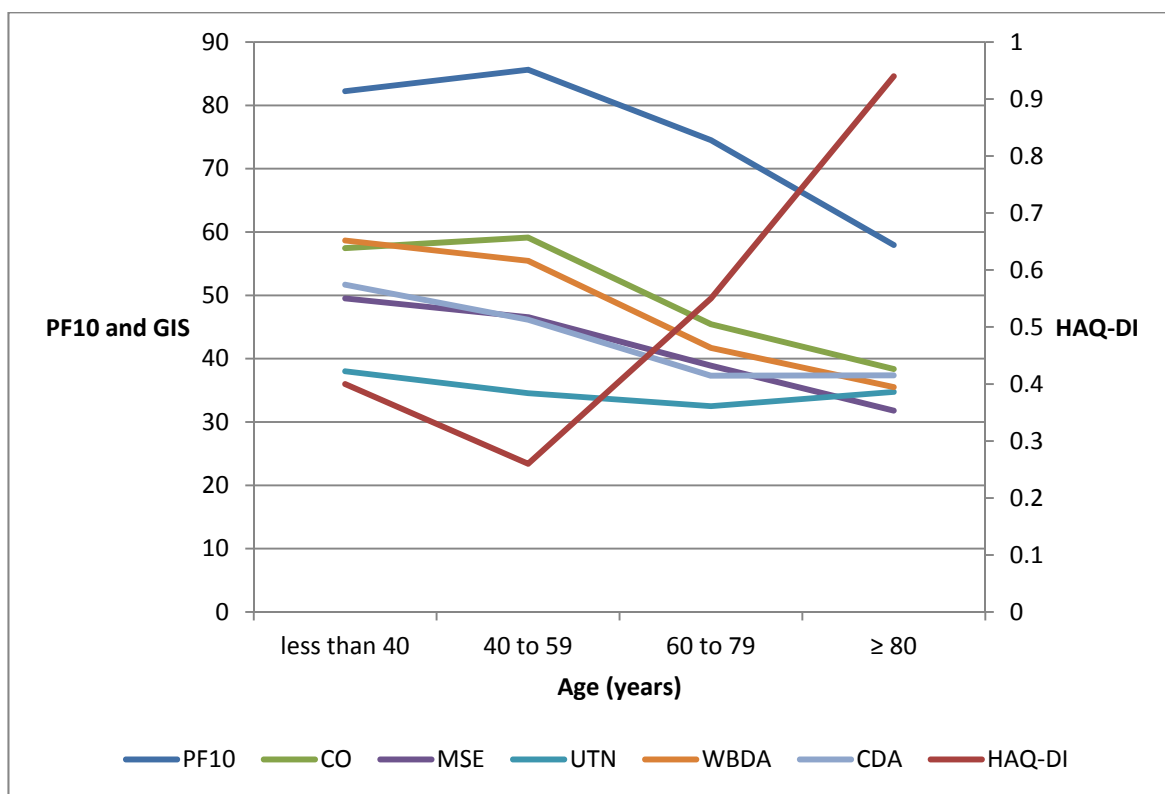


Table 6-9: HRQOL in participants grouped by socio-demographic characteristics (categorical)

		Mean PF 10 (95% CI)	Mean HAQ- DI (95% CI)	Mean CO (95% CI)	Mean MSE (95% CI)	Mean UTN (95% CI)	Mean WBDA (95% CI)	Mean CDA (95% CI)
Frequency of alcohol intake	Daily	82.20 (79.06, 85.35)	0.35 (0.29, 0.42)	44.49 (41.12, 47.86)	36.88 (33.90, 39.87)	31.17 (28.82, 33.52)	42.54 (39.61, 45.47)	36.55 (33.78, 39.31)
	3-4 time/ week	83.40 (80.35, 86.45)	0.28 (0.21, 0.35)	48.69 (45.22, 52.17)	41.76 (38.62, 44.91)	30.24 (27.89, 32.59)	44.72 (41.49, 47.94)	39.08 (36.28, 41.89)
	1-2 times/ week	79.96 (76.63, 83.30)	0.41 (0.33, 0.49)	50.68 (47.29, 54.07)	40.50 (37.35, 43.64)	33.42 (30.61, 36.24)	46.44 (43.18, 49.69)	42.44 (39.37, 45.52)
	1-3 times/ month	74.54 (69.20, 79.88)	0.52 (0.38, 0.65)	46.46 (41.04, 51.89)	41.19 (35.84, 46.54)	33.41 (29.52, 37.30)	45.95 (40.59, 51.31)	38.23 (33.74, 42.73)
	Special occasions	62.37 (57.81, 66.94)	0.89 (0.74, 1.03)	49.61 (45.08, 54.13)	40.38 (35.75, 45.02)	38.56 (35.19, 41.93)	43.75 (39.27, 48.23)	40.99 (36.74, 45.24)
	Never	56.36 (51.22, 61.49)	1.09 (0.93, 1.25)	56.75 (50.87, 62.64)	47.38 (41.57, 53.19)	39.28 (34.62, 43.94)	52.17 (46.73, 57.61)	48.24 (43.11, 53.38)
P value for ANOVA		< 0.01	<0.01	0.005	0.024	<0.01	0.041	0.001
MDI neighbourhood deprivation	Most deprived	64.67 (60.24, 69.10)	0.78 (0.66, 0.90)	57.74 (53.68, 61.80)	46.53 (42.66, 50.39)	36.19 (33.14, 39.24)	51.46 (47.73, 55.18)	49.37 (45.66, 53.08)

		Mean PF 10	Mean HAQ-	Mean CO	Mean MSE	Mean UTN	Mean WBDA	Mean CDA	
		(95% CI)	DI (95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	
	Second most deprived	74.08 (70.35, 77.81)	0.53 (0.44, 0.62)	49.44 (45.96, 52.92)	40.09 (36.77, 43.41)	35.69 (32.96, 38.43)	44.58 (41.08, 48.07)	39.92 (36.65, 43.18)	
	Mid -deprived	78.88 (75.36, 82.39)	0.44 (0.35, 0.52)	44.43 (40.86, 48.00)	38.33 (34.85, 41.80)	30.77 (28.20, 33.34)	42.46 (39.10, 45.82)	37.50 (34.49, 40.51)	
	Second least deprived	79.85 (76.61, 83.10)	0.40 (0.32, 0.48)	46.30 (42.77, 49.83)	38.73 (35.51, 41.96)	31.75 (29.15, 34.36)	43.49 (40.27, 46.71)	37.62 (34.73, 40.51)	
	Least deprived	79.27 (75.77, 82.76)	0.43 (0.35, 0.52)	46.85 (43.20, 50.50)	39.40 (36.03, 42.77)	33.28 (30.61, 35.95)	44.72 (41.39, 48.04)	37.75 (34.87, 40.63)	
	P value for ANOVA	<0.01	< 0.01	<0.01	0.009	0.022	0.005	< 0.01	
	BMI	≤18.4	71.85 (46.78, 96.93)	0.68 (0.06, 1.29)	50.00 (30.68, 69.32)	47.73 (27.22, 68.23)	35.00 (23.83, 46.17)	43.54 (25.23, 61.84)	38.64 (21.14, 56.13)
		18.5 to 24.9	76.76 (72.85, 80.67)	0.42 (0.32, 0.51)	44.95 (41.02, 48.89)	37.69 (34.14, 41.25)	33.40 (30.44, 36.36)	44.82 (41.11, 48.53)	37.80 (34.54, 41.07)
		25 to 29.9	80.90 (78.54, 83.26)	0.42 (0.36, 0.47)	48.25 (45.75, 50.75)	39.97 (37.60, 42.34)	33.09 (31.23, 34.95)	42.35 (40.01, 44.69)	38.89 (36.73, 41.05)
		≥30	71.09	0.65	52.25	43.11	33.71 20.51	49.63	43.43

		Mean PF 10 (95% CI)	Mean HAQ-DI (95% CI)	Mean CO (95% CI)	Mean MSE (95% CI)	Mean UTN (95% CI)	Mean WBDA (95% CI)	Mean CDA (95% CI)
		(68.17, 74.02)	(0.57, 0.73)	(49.44, 55.06)	(40.50, 45.73)	(31.60, 35.81)	(47.03, 52.24)	(41.00, 45.85)
P value for ANOVA		<0.01	< 0.01	0.023	0.073	0.969	0.001	0.017
Age (years)	< 40	82.24 (69.26, 95.23)	0.40 (0.09, 0.71)	57.45 (44.17, 70.73)	49.50 (36.05, 62.95)	38.00 (29.23, 46.77)	58.65 (48.20, 69.11)	51.68 (39.28, 64.08)
	40 to 59	85.63 (83.04, 88.22)	0.26 (0.20, 0.32)	59.11 (56.06, 62.16)	46.55 (43.81, 49.29)	34.55 (32.39, 36.71)	55.45 (52.74, 58.17)	46.15 (43.65, 48.65)
	60 to 79	74.50 (72.31, 76.70)	0.55 (0.49, 0.60)	45.43 (43.31, 47.55)	38.89 (36.83, 40.94)	32.49 (30.86, 34.13)	41.70 (39.76, 43.63)	37.31 (35.45, 39.16)
	≥80	57.95 (53.40, 62.49)	0.94 (0.81, 1.08)	38.37 (34.34, 42.39)	31.80 (27.84, 35.76)	34.74 (31.07, 38.41)	35.51 (30.92, 40.09)	37.35 (33.26, 41.44)
P value for ANOVA		<0.01	< 0.01	< 0.01	<0.01	0.261	< 0.01	< 0.01

Abbreviations: CI: Confidence Interval; PF-10: Physical Function 10; HAQ-DI: Health Assessment Questionnaire Disability Index; GIS CO: Gout Impact Scale Concern Overall; MSE: Medication Side Effects; UTN: Unmet Treatment Need; WBDA: Wellbeing During Attack; CDA: Concern During Attack. MDI; Multiple Deprivation Indices, BMI; Body Mass Index, ANOVA; Analysis of Variance

6.6 Discussion

Poor generic (PF-10, HAQ-DI) and gout-specific (GIS) HRQOL was associated with currently having an attack of gout, a history of oligo or polyarticular attacks and higher frequency of attacks over the last 12 months. The association of allopurinol, its dose and SUA > 360 $\mu\text{mol/L}$ with HRQOL was variable. Although treatment with allopurinol (compared to not taking allopurinol) was associated with better HRQOL (lower unmet treatment need) in the GIS, those on allopurinol > 300 mg per day reported worse HRQOL in the generic questionnaires as well as higher GIS concern for gout and greater concern in the treatment sub-scales. SUA above the treatment target (> 360 $\mu\text{mol/L}$ compared to SUA \leq 360 $\mu\text{mol/L}$) was associated with GIS unmet treatment need only. No association was seen between HRQOL and tophi.

Responders with co-morbid conditions such as ischaemic heart disease, stroke, anxiety, depression, body pain and renal failure reported poorer HRQOL in all three questionnaires (PF-10, HAQ-DI and GIS). Responders with self-reported diabetes, hypertension and TIA reported lesser impact of gout on HRQOL in the GIS. Increasing age was associated with worse HRQOL in the generic questionnaires but better HRQOL in the GIS. BMI < 18.5 and \geq 30 was associated with worst HRQOL compared to other BMI groups. Living in the most deprived neighbourhood (compared to other neighbourhoods) and not drinking alcohol (compared to daily alcohol consumption) were associated with worst HRQOL. Female gender (compared to male), further education (compared to no further education) and age < 21 at leaving further education (compared to age > 21) were associated with poor generic and gout-specific HRQOL. Being non-Caucasian and living alone or not being married was associated with poor HRQOL in the GIS only.

The association of allopurinol > 300 mg per day with poor HRQOL may be secondary to confounding by indication - it is plausible that those requiring doses > 300 mg per day (3.8% of

participants) had a more severe form of gout which may influence the outcome (HRQOL) at the outset. SUA above treatment target ($> 360 \mu\text{mol/L}$) led to poorer gout-specific HRQOL (higher GIS concern overall and unmet treatment need). Hyperuricaemia underpins the pathogenesis of gout (Taylor, Schumacher et al. 2007) and is associated with frequency of attacks (Li-Yu, Clayburne et al. 2001). Uncontrolled hyperuricaemia may reflect sub-optimal treatment (unmet treatment need) and recurrent attacks leading to irreversible joint damage and disability (concern overall for gout). Although no association was seen between tophi and HRQOL, tophi are a direct marker for total body urate and act as indicator of disease severity (Taylor, Schumacher et al. 2007). The lack of impact of tophi on HRQOL in this study may be explained by the low prevalence of tophi (2.3%) documented by healthcare professionals in the medical records. Physical measurement of tophi by non-specialists in a primary care setting may come with an inevitable risk of under-recognition and / or under-recording.

The impact of co-morbid conditions on HRQOL may be linked to their well-recognised association with gout (Brixner, Ho 2005). It is plausible that co-morbidities become more prevalent in severe gout – a cluster analysis of co-morbid conditions in gout revealed that obesity, hypertension, dyslipidaemia and metabolic syndrome increased with gout duration, independent of age and gender (Richette, Clerson et al. 2013). Although causality between severity of gout and co-morbidity could not be established due to the cross-sectional design of this study, it may be that co-morbid conditions worsen with progressive gout (Richette, Clerson et al. 2013), thereby impacting on HRQOL. The association of co-morbidities with HRQOL presented in this chapter however does not take into consideration potential confounding factors. It is likely that responders with co-morbidities are older or are more likely to be treated with ULT. A plausible explanation for the better HRQOL in the GIS seen in the presence of diabetes or hypertension may include surveillance bias (as co-morbid conditions require long-term medical care) and that

people with gout perceive their other medical problems as more 'serious' (therefore prioritising other medical conditions over gout in affecting their HRQOL). Patients with poor health or non-health competing demands may prioritise symptomatic conditions which exacerbate their functional limitations (Zulman, Kerr et al. 2010), over a relapsing remitting condition such as gout which can have long inter-critical periods.

Although older persons reported worse generic HRQOL (PF-10 and HAQ-DI items focus on physical functioning), they may attribute joint pain and disability to the natural ageing process and may not expect treatment to cause a significant improvement in their symptoms. These beliefs may reflect the lower unmet treatment need in this age group. Females with gout generally are older (Harrold, Yood et al. 2006) and may therefore have poorer generic HRQOL compared to men. Co-morbid conditions such as hypertension, heart and renal failure are well associated with gout in females (Puig, Michan et al. 1991), all of which may also contribute to poor HRQOL in the unadjusted analysis in this chapter. Adults (age > 21 years) with further education may have a better insight into their condition, thereby reporting better HRQOL compared to younger adults without further education. It is possible that poor HRQOL reported by non-Caucasian people may be attributed to an earlier onset or a more severe form of gout based on their genetic susceptibility to metabolic diseases, or that their views are influenced by their own previous experiences and that of their family or community members (Dalbeth, Petrie et al. 2011). Poor access to health care resources by ethnic minorities in the UK due to linguistic or cultural barriers have been described previously (Szczepura 2005). Moderate alcohol intake has been shown to reduce the risk of cardiovascular disease (Saremi, Arora 2008) and ischaemic stroke (Djousse, Ellison et al. 2002). Moderate alcohol intake has also led to an improvement in HRQOL in studies of young and older adults (Byles, Young et al. 2006; Saito, Okamura et al. 2005) and is deemed a protective factor for improved health in those with and without chronic musculoskeletal pain

(Arvidsson, Arvidsson et al. 2008). Alcohol may also be seen as a stress reliever and promote social integration, both of which may lead to an improvement in HRQOL (Kim, Vincent et al. 2013).

6.6.1 Comparison to existing studies

The overall generic HRQOL in the HAQ-DI and PF-10 is only mildly impaired in this study, which is consistent with previous findings. Median HAQ-DI scores have varied from 0.13 (identical to that found in this study) in a cohort study of participants with primary gout in Mexico (Vazquez-Mellado, Cruz et al. 2006) to 0.30 in a study based in mixed settings of a veterans affairs medical centre, university hospital and community rheumatology practice (Khanna, Ahmed et al. 2008). By consensus a mean (SD) HAQ-DI 0.51 (0.71) represents mild disability only (Krishnan, Tugwell et al. 2004). Although no specific cut-offs exist to define poor HRQOL in the PF-10, a score near 100 indicates good health and functional capacity. UK normative PF-10 scores for adult men range from 80 to 93.9 and for adult women from 74.8 to 92.9 (Jenkinson, Coulter et al. 1993). Any discrepancy between the HRQOL in this and other studies may reflect differences in the sampling frame. Other studies may have included populations with the diagnosis of gout based on the identification of urate crystals, complex or severe gout treated in secondary care, refractory to treatment with conventional ULT and high levels of SUA (Ten Klooster, Oude Voshaar et al. 2011; Becker, Schumacher et al. 2009; Hirsch, Terkeltaub et al. 2010). Other plausible explanations for the differences in HRQOL between this study and others include variations in the methods of scoring, for example, the exclusion of domains pertaining to help from others and the use of aids and devices in the study by Vazquez-Mellado et al (Vazquez-Mellado, Cruz et al. 2006).

The results of HRQOL stratified by responders' gout characteristics had variable concordance with other studies. Just as in this study, increasing attack frequency had the strongest association with

GIS in a community validation study (Hirsch, Terkeltaub et al. 2010) and with Short Form-12 Physical and Mental Component Summary in a cross-sectional study of people with self-reported gout across Europe and the USA (Khanna, Nuki et al. 2012). A history of oligo or polyarticular attacks led to worse HRQOL in all questionnaires (except unmet treatment need) in this study. Although polyarticular gout led to poorer HRQOL in the SF-36 (Khanna, Perez-Ruiz et al. 2011; Lee, Hirsch et al. 2009), correlations between the number of joints involved in an attack and the GIS were minimal to small in another study (Hirsch, Terkeltaub et al. 2010). There were no existing studies reporting the influence of currently having an attack of gout on HRQOL, that could be used to compare the poor HRQOL seen in the presence of a gout attack at the time of questionnaire completion in this study. The presence of typical attack pain in the past 3 months was moderately correlated with well being during attack and concern overall in one study (Hirsch, Lee et al. 2008).

This study highlights the impact of co-morbidities on generic as well as gout-specific HRQOL using the PF-10, HAQ-DI and GIS, which have not been used together in a primary care setting previously. A few existing studies imply that co-morbid conditions adversely affect physical HRQOL more than the psychological HRQOL (Singh, Strand 2008; Roddy, Zhang et al. 2007c; Lee, Hirsch et al. 2009). Qualitative studies have shown that those with gout experience pain, isolation and stigmatisation (Lindsay, Gow et al. 2011), yet there are no studies to examine the impact of anxiety and depression in gout on HRQOL. Worse generic but better GIS HRQOL in older participants in this study has been seen previously. The association of older age with poor generic HRQOL in this study has also been found previously in a UK primary care-based cross-sectional survey (Roddy, Zhang et al. 2007c). Non-Caucasian ethnicity was associated with higher illness perception in a New Zealand based study (Dalbeth, Petrie et al. 2011), similar to the poor GIS HRQOL seen amongst non-Caucasians in this study.

6.6.2 Strengths of the study

This is the first study based in primary care in the UK to assess HRQOL in those with gout using a combination of generic and gout-specific questionnaires. The use of PF-10, HAQ-DI and GIS together provides a comprehensive picture of the impact of gout and other characteristics on HRQOL. Although validated for measuring functional disability in gout at OMERACT 10 (Singh, Taylor et al. 2011), the HAQ-DI does not measure the impact of gout on psychosocial well being. Hence certain independent variables which may not be directly linked to physical functioning (such as ethnicity and accommodation) are associated (unadjusted univariate analysis only) with HRQOL only in the GIS.

The robustness of the analyses which led to the study findings is evident through the choice of statistical tests. Given an adequate sample size of 1184, the 'central limit theorem' of normal distribution (Bland 2000) was assumed to be true. This assumption was key to the use of parametric tests, which are more likely to detect a small yet significant statistical difference between the means of two or more groups. Whilst the independent samples t-test was appropriate to compare the means of groups based on independent variables with dichotomous outcomes, it was not suitable for groups with multiple (ordinal) outcomes. Using the t-test in the latter situation would have created numerous comparisons based on the presence of many groups. The greater the number of groups, the greater the likelihood of getting a statistically significant difference even though the null hypothesis is true (population means are the same) (Bland 2000). Hence a better way to assess differences between groups based on multiple outcomes was ANOVA, which compared the variation between groups to that of within groups (Bland 2000).

6.6.3 Limitations of the study

All associations in this chapter reflect a statistically significant difference between the mean HRQOL scores stratified by responders' gout, co-morbid and socio-demographic characteristics but there are no adjustments for potential (measured) confounding factors. The cross-sectional design of the study precludes any causality to be established between the independent variables (gout-specific, co-morbid, socio-demographic characteristics) and the outcome (HRQOL) but merely allows the testing of associations between the two. Although useful in detecting the association of certain gout and socio-demographic characteristics with HRQOL, the GIS has yet to be fully validated by the OMERACT group (Singh, Taylor et al. 2011) and as such it may not be considered as reliable a patient-reported outcome measure as the OMERACT-endorsed HAQ-DI or SF-36.

6.6.4 Implications for clinical practice and further research

In addition to the impact on generic HRQOL as previously seen (Schlesinger 2011), gout, co-morbid and socio-demographic characteristics affect gout-specific HRQOL. Hence it is important that health care professionals identify those at risk of poor outcome (frequent attacks, a history of oligo or polyarticular attacks, SUA above the treatment target, multiple co-morbidities, females, non-Caucasians, those living in deprived areas and those without further education) and offer them urate-lowering treatment as well as address their co-morbidities. Despite having overall low mean unmet treatment needs, participants' concern for gout overall and during acute attacks remains high. This may imply that patients with gout are unaware of the role of ULT or have low expectations from treatment, both of which may be addressed through patient education.

The unadjusted association between explanatory variables and HRQOL has informed the plan of analysis in the next chapter. The robustness of the associations seen between gout, co-morbid

and socio-demographic characteristics and HRQOL will be tested in the next chapter in the thesis using multivariate linear regression models that adjust for potential confounders.

6.7 Conclusion

In conclusion, this chapter presents the mean generic and gout-specific HRQOL for participants with gout. It then examines the differences between the HRQOL scores stratified by gout-specific, co-morbid and socio-demographic characteristics (explanatory variables). It highlights that HRQOL is poor in the presence of certain gout, co-morbid and socio-demographic characteristics. The association of these explanatory variables on HRQOL however is unadjusted for confounding by each other in this chapter. The next chapter presents the associates of poor HRQOL using a linear regression model, unadjusted and multivariate adjusted for confounding factors.

7 The cross-sectional associations of gout-specific, co-morbid and socio-demographic characteristics with Health Related Quality of Life: a linear regression analysis

7.1 Introduction

The previous chapter compared the mean Health Related Quality of Life (HRQOL) (Physical Function 10, PF-10, Health Assessment Questionnaire Disability Index, HAQ-DI and Gout Impact Scale, GIS) scores of participants stratified by gout-specific, co-morbid and socio-demographic characteristics. The comparisons between the mean HRQOL scores however were univariate in nature and did not take into account the influence of a third factor or a confounder, related to the exposure (above mentioned independent variables) and the outcome (HRQOL). This chapter examines which variables have an independent association with HRQOL, through linear regression models which take into account any confounding factors.

7.2 Aim

The aim of this chapter is to identify which gout, co-morbid and socio-demographic-related factors are independently associated cross-sectionally with HRQOL.

7.3 Objective

To identify associations between HRQOL and gout-specific, co-morbid and socio-demographic characteristics, both unadjusted and adjusted for confounding explanatory variables.

7.4 Methods

The source of data used in this chapter is the baseline phase of the cohort study of HRQOL in gout and medical record review of consenting participants. The sampling frame (inclusion and

exclusion criteria), recruitment of participants (mailing process), contents of the questionnaire and categories and subscales and items of the HRQOL measures (PF-10, HAQ-DI and GIS) are described in chapter 4 (Study design and methods). The scoring and interpretation of the HRQOL measures is described in sections 6.3.4 and 6.4.2 in chapter 6 (The association of gout, co-morbid and socio-demographic characteristics on Health Related Quality of Life: Univariate analysis). The sections below describe the methods specific to the univariable and multivariable adjusted regression analyses.

7.4.1 HRQOL scores

HRQOL scores were left unchanged as continuous interval scales based on the assumption that there is an underlying continuum of functional limitation, disability and impact of gout in the PF-10, HAQ-DI and GIS respectively. Arbitrary dichotomisation at the median value has been previously shown to lead to a loss of power equivalent to discarding a third of the data (MacCallum, Zhang et al. 2002). Although multiple definitions of disability exist in the HAQ-DI ranging from >0 (Krishnan, Sokka et al. 2004) to the 95th percentile (Sokka, Krishnan et al. 2003) and a score of ≥ 1 in normative populations (Sokka, Krishnan et al. 2003), there are 25 possible values (Bonnie, Fries 2003) and hence it was treated as a continuous scale. HRQOL were entered into univariable and multivariable linear regression models as the dependent variables.

7.4.2 Explanatory gout-specific variables

The following variables had dichotomous response options: current attack of gout, a history of oligo or polyarticular attacks, treatment with allopurinol and presence of tophi. Frequency of attack and the dose of allopurinol were self-reported in ordinal categories. SUA, a continuous variable, was dichotomised using $360 \mu\text{mol/L}$ as the cut-off point. The level of SUA is considered a surrogate for joint tissue urate level (Zhang, Doherty et al. 2006a). A level of $\leq 360 \mu\text{mol/L}$

reflects a tissue level that is below the saturation point for formation of urate crystals and encourage crystal dissolution (Zhang, Doherty et al. 2006a). There is clinical evidence to support the linear relationship between the level of SUA and tophi (Perez-Ruiz, Calabozo et al. 2002c), with a significant reduction in the number of tophi at SUA < 370 $\mu\text{mol/L}$ (Mccarthy, Barthelemy et al. 1991). By maintaining a SUA < 360 $\mu\text{mol/L}$ for 12 months, a reduction in the urate crystal load in knee synovial fluid was seen (Li-Yu, Clayburne et al. 2001). Hence to achieve the aim of cure of urate lowering treatment, SUA must be maintained at a level of $\leq 360 \mu\text{mol/L}$ (Zhang, Doherty et al. 2006a), which is the cut-off point used in this study. In order to minimise cases with missing data pertaining to the dose of allopurinol, only those who had responded yes to treatment with allopurinol were included in the linear regression models for allopurinol. Similarly only those who consented for medical record review were included in the regression models for SUA and tophi.

7.4.3 Explanatory co-morbid characteristics

Stroke, transient ischaemic attack (TIA), angina, myocardial infarction (MI), renal calculi, renal failure, hypertension, hyperlipidaemia, diabetes and generalised body pain were self-reported by ticking the corresponding box to indicate the presence of the condition. Continuous scores of anxiety in the Generalised Anxiety Disorder-7 (GAD-7) and depression in the Patient Health Questionnaire-9 (PHQ-9) were categorised into severity groups using validated cut-off points (Spitzer, Kroenke et al. 2006; Kroenke, Spitzer 2002).

7.4.4 Explanatory socio-demographic variables

Gender and self-reported attendance at further education had binary response options were left unchanged. Self-reported categorical frequency of alcohol consumption was also left unchanged. Age, self-reported as a continuous scale, was categorised into less than 40, between 40 and 80 divided into 20-year age bands and greater than 80 years. Body Mass Index (BMI) comprising of

self-reported continuous height and weight was categorised into previously validated World Health Organisation classification groups (WHO Expert Consultation 2004). Neighbourhood deprivation rank (Multiple Deprivation Indices, MDI) scores were divided into quintiles. The following self-reported nominal variables were dichotomised: ethnicity and relationship status.

7.5 Statistical analyses

The ascertainment of self-reported explanatory variables (gout, co-morbid and socio-demographic) in the questionnaire as well as SUA and tophi from medical record review has been described in Chapter 5 (Cross-sectional survey of Health Related Quality of Life in gout: Response and responder characteristics). The categorisation of continuous explanatory variables has been described in section 6.4 of chapter 6 (The association of gout, co-morbid and socio-demographic characteristics with Health Related Quality of Life: Univariate analysis). The subscales of the GIS as well as the categories and number of items of the HAQ-DI and PF-10 have been described in sections 4.2.4 (impact of gout on quality of life) and 4.2.5 (general health and co-morbidity) in chapter 4 (Study design and methods). Scoring of the three HRQOL questionnaires and the interpretation of these scores has been described in section 6.3.4 and 6.4.2 in chapter 6 (The association of gout, co-morbid and socio-demographic characteristics with Health Related Quality of Life: Univariate analysis). The following explanatory variables were used in the univariable and multivariable regression models:

Table 7-1: Explanatory variables used in linear regression models

Gout	Co-morbid	Socio-demographic
Frequency of attack	Diabetes	Age
Current gout attack	Stroke	Gender
Oligo-polyarticular attacks	Hypertension	Neighbourhood deprivation
Treatment with allopurinol	TIA	Ethnicity
Dose of allopurinol	Hyperlipidaemia	BMI
Tophi	Kidney failure	Further education
Disease duration	MI	Alcohol frequency
Serum uric acid	Kidney stones	Relationship status
	Angina	
	Body pain	
	Anxiety	
	Depression	

Abbreviations: TIA: transient ischaemic attack; MI: Myocardial Infarction; BMI: body mass index

Outcome variables were the PF-10, HAQ-DI and GIS. All statistical analyses were performed using SPSS version 21 (SPSS Inc., Chicago, IL).

7.5.1 Testing for normality of dependent variables

Although the sample size ($n = 1184$) of responders in the cross-sectional study was large enough to have normally distributed HRQOL scores, the normality of the observed data was assessed using measure of skewness as well as visually through histograms and Quantile-Quantile (Q-Q) plots (see appendix 19). An absolute value of skewness > 2 is used as a reference for significant non-normality of data (Hoyle 1995). The mean, median and measure of skewness are presented in Table 7-2 below. Although the distributions for the PF-10 and HAQ-DI are negatively and positively skewed respectively, the absolute value of skewness is less than 2. Hence the data are considered to be normally distributed. The sub-scales of the GIS had means and medians which were similar in values and the distribution of the data were considered close to normal distribution.

Table 7-2: Measures of dispersion of the dependent variables

(Total number of participants included in the analysis n=851)

	PF-10	HAQ-DI	GIS CO	MSE	UTN	WBDA	CDA
Mean	75.29	0.46	46.99	39.79	32.59	45.54	39.32
Median	90	0	50	37.5	33.33	45.45	37.5
Skewness	-0.90	1.63	-0.03	0.32	0.55	0.09	0.19

Abbreviations: PF-10: Physical Function 10; HAQ-DI: Health Assessment Questionnaire Disability Index; GIS: Gout Impact Scale; CO: Concern Overall; MSE: Medication Side Effects; UTN: Unmet Treatment Need; WBDA: Wellbeing During Attack; CDA: Concern During Attack.

7.5.2 Parametric tests for testing the associations between HRQOL (continuous) and independent variables (dichotomous or ordinal)

7.5.2.1 Linear regression as a test for association

Univariable linear regression model was used to test for an association between a continuous variable (HAQ-DI, PF-10 and GIS) and the following dichotomous or ordinal independent variables:

1. Gout-specific characteristics (currently having an attack of gout, oligo or polyarticular attacks, frequency of attack, treatment with allopurinol, dose of allopurinol, disease duration, tophi, SUA level)
2. Co-morbid conditions (diabetes, hypertension, hyperlipidaemia, MI, angina, stroke, transient ischaemic attack, renal impairment, renal calculi, any body pain, anxiety and depression)
3. Socio-demographic characteristics (age, gender, ethnicity, further education, alcohol intake, neighbourhood deprivation ranking, relationship status, BMI).

In the univariable regression model, the following equation was used:

$$y = \beta_0 + \beta_1 X \text{ (Szklo, Nieto 2014)}$$

where “y” is the predicted value of the dependent continuous variable (PF-10, HAQ-DI and GIS), β_0 is the intercept (estimated value of y when x is 0) and β_1 is the regression coefficient (estimated increase in y per unit increase in the independent variable x) (Szklo, Nieto 2014). The regression coefficient denotes the strength of association between the independent variable and the HRQOL scores (how much increase or decrease in score is expected or predicted as the independent variable changes or increases per unit of measurement). Each independent variable was entered one by one into the linear regression model (one each for PF-10, HAQ-DI and each of the 5 sub-scales of the GIS). The association between the two variables is considered statistically significant if $p < 0.05$.

However a univariable model does not take into account the role of potential confounding factors (characteristics other than that under assessment). Stratified analysis was not feasible in this case as there are at least 12 potential confounders (assuming co-morbidity as a single factor) with a range of 2 (for dichotomous variables such as gender) to 10 strata (for number of co-morbidities) each. The total number of strata to allow for possible combinations of independent variables would be 3072000. Instead multivariable analysis was used, which allowed to control for all of these confounders simultaneously. The following equation denotes the predicted value of HRQOL scores (y) when there is a change or increase in the independent variable (x1) after controlling for multiple other independent variables (x2, x3 etc.)

$$y = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 \text{ (Szklo, Nieto 2014)}$$

All gout-specific variables in the univariable model were entered into multivariable models which also included (and hence adjusted for) the following confounding variables:

- I. Socio-demographic characteristics
- II. Socio-demographic and co-morbid characteristics

This model was based on the assumption that there is no interaction between the numerous independent variables, and that change in HRQOL scores for a unit change in one independent variable (attack frequency for example) is constant for the entire range of another independent variable (age for example) (Szklo, Nieto 2014). Therefore, interaction terms have not been included in the multiple regression models. In order to maximise the number of participants included in the regression analyses, pairwise deletion on SPSS (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) was selected in preference to the default option of listwise deletion. As opposed to listwise deletions (which only include cases with a full set of data), the advantage of using this method is that those cases with data missing for some variables can still be utilised in the regression models analysing other variables with non-missing values. Data for all variables are assumed to be missing at random and unrelated to the observed values.

7.5.3 Variables with high levels of missing data and modifications to the linear regression models

Linear regression analyses were modified where appropriate in order to reduce the levels of missing data or correlations. For example, serum uric acid (SUA) were only available in the medical records of 461 (42.7%) of the 1078 participants who agreed for medical record review (1079 consented to MRR initially but one participant withdrew at a later stage). Hence linear regression analyses were restricted to those who had a record of SUA (461 participants). The regression analyses of tophi as the independent variable were also restricted to the 1078 participants who had consented to medical record review. The dose of allopurinol was only available for 616 (52%) of the 1184 participants (as not all participants were taking allopurinol). Hence linear regression for the dose of allopurinol was restricted to the participants who took allopurinol (n=630). For multivariate analyses the following models were used:

1. Adjusted for socio-demographic, co-morbid and gout characteristics except SUA, tophi and dose of allopurinol
2. Adjusted for socio-demographic, co-morbid and SUA
3. Adjusted for socio-demographic, co-morbid and tophi
4. Adjusted for socio-demographic, co-morbid and dose of allopurinol.

In order to be considered valid, associations had to be statistically significant after adjustments made for gout characteristics in all four multivariable models. The results in Table 7-3 to Table 7-5 below are presented for model 1 and any changes in associations in models 2 to 4 are listed in the footnotes.

7.6 Results

The results are presented individually for each HRQOL questionnaire used in the study.

7.6.1 PF-10

HRQOL measured by the PF-10 was associated with the following gout characteristics in the univariate analysis: frequency of attacks over the past 12 months, current attack of gout, a history of oligo or polyarticular attacks, and the dose of allopurinol. The β coefficient values and their 95% CI are presented in Table 7-3. After adjustments for other gout, co-morbid and socio-demographic characteristics in the multivariate analysis however, only frequency of attacks remained independently associated with HRQOL in the PF-10 (reduced strength of association). No association was seen between HRQOL measured with the PF-10 and treatment with allopurinol, disease duration and SUA in the univariate or multivariate analyses.

The following co-morbid conditions were associated with poorer HRQOL in the PF-10 in the univariate analysis (see Table 7-3): diabetes, stroke, hypertension, renal failure, myocardial infarction, angina, generalised body pain, anxiety and depression. After adjustments for gout,

other co-morbid and socio-demographic characteristics in the multivariate analysis however, only angina, body pain and depression remained independently associated with HRQOL in the PF-10. The strength of association of these explanatory variables with HRQOL in the PF-10 was however reduced in the adjusted analysis, as evident by the corresponding β coefficients and 95% CI in Table 7-3. No associations were seen between HRQOL in the PF-10 and TIA, hyperlipidaemia and renal calculi in the univariate or multivariate analyses.

The following socio-demographic characteristics were associated with poorer HRQOL in the PF-10 in the univariate analysis (see Table 7-3): increasing age, female gender, neighbourhood deprivation, increase in BMI, lack of further education and less frequent alcohol consumption. After adjustment for other socio-demographic, co-morbid and gout characteristics only age, gender and frequency of alcohol consumption remained independently associated with HRQOL in the PF-10. The strength of association between HRQOL in the PF-10 and age did not alter after adjustments in the multivariate analysis. No association was seen between HRQOL in the PF-10 and ethnicity or relationship status in the univariate or multivariate analyses.

Table 7-3: The association of HRQOL in the PF-10 with gout-related, co-morbid and socio-demographic characteristics

	Unadjusted β (95% CI)	N	Adjusted β^{26} (95% CI)	n
Gout characteristics				
Frequency of attack	-3.50 (-4.46, -2.53)	910	-1.37 (-2.31, -0.44)	551
Current gout attack	13.78 (8.58, 18.97)	921	-0.92 (-5.52, 3.67)	551
Oligo-polyarticular attacks	9.13 (5.71, 12.56)	919	2.26 (-0.67, 5.19)	551
Treatment with allopurinol	1.67 (-1.75, 5.10)	910	2.00 (-0.83, 4.83)	551
Dose of allopurinol	8.41 (4.29, 12.53)	472	2.53 (-0.67, 5.72)	327
Tophi	-7.94 (-19.26, 3.38)	856	-5.14 (-14.02, 3.75)	581
Disease duration	0.71 (-0.72, 2.14)	955	1.09 (-0.12, 2.30)	551
Serum uric acid	1.41 (-4.63, 7.45)	379	-0.86 (-5.75, 4.04)	256
Co-morbid characteristics			Adjusted β^{27} (95% CI)	
Diabetes	-11.35 (-15.67, -7.03)	958	-2.66 (-6.29, 0.97)	603
Stroke	-17.33 (-26.79, -7.88)	958	-7.35 (-15.16, 0.46)	
Hypertension	-8.19 (-11.56, -4.82)	958	0.65 (-2.35, 3.65)	
TIA	-0.18 (-7.62, 7.25)	958	3.08 (-3.04, 9.20)	
Hyperlipidaemia	-2.96 (-6.30, 0.39)	958	1.49 (-1.36, 4.35)	
Kidney failure	-18.29 (-26.01, -10.58)	958	-3.98 (-10.27, 2.30)	
MI	-11.82 (-17.28, -6.36)	958	-2.11 (-6.81, 2.58)	
Kidney stones	1.49 (-5.07, 8.05)	958	6.36 (1.10, 11.62) ²⁸	
Angina	-16.59 (-21.50, -11.68)	958	-6.17 (-10.46, -1.87)	
Body pain	18.44 (14.75, 22.12)	783	9.39 (6.43, 12.35)	

²⁶ Adjusted for socio-demographic and co-morbid characteristics.²⁷ Adjusted for gout (except SUA, tophi and dose of allopurinol) and socio-demographic characteristics.²⁸ After adjusting for allopurinol dose, kidney stones were not associated with PF-10 (β 4.02, 95% CI -2.30, 10.33)

	Unadjusted β (95% CI)	N	Adjusted β^{26} (95% CI)	n
Anxiety	-12.61 (-14.68, -10.55)	886	-0.40 (-2.96, 2.15)	
Depression	-13.98 (-15.58, -12.38)	840	-10.74 (-12.89, -8.59)	
Socio-demographic characteristics			Adjusted β^{29} (95% CI)	
Age	-11.61 (-13.96, -9.26)	958	-11.10 (-13.37, -8.83)	603
Gender	-21.30 (-25.57, -17.03)	958	-11.17 (-15.10, -7.24)	
Neighbourhood deprivation	3.24 (2.08, 4.40)	958	1.08 (0.13, 2.04) ³⁰	
Ethnicity	0.45 (-7.03, 7.93)	958	0.54 (-5.53, 6.62)	
BMI	-3.28 (-5.56, -1.01)	900	-1.48 (-3.29, 0.34)	
Further education	-10.10 (-14.13, -6.07)	914	-2.64 (-5.88, 0.60)	
Alcohol frequency	-5.34 (-6.31, -4.37)	944	-1.96 (-2.84, -1.08)	
Relationship status	2.04 (-1.94, 6.03)	958	0.52 (-2.75, 3.79)	

Abbreviations: TIA: CI: Confidence Interval; Transient Ischaemic Attack; MI: Myocardial Infarction; BMI: Body Mass Index

²⁹ Adjusted for gout (except SUA, tophi and dose of allopurinol) and co-morbid characteristics.

³⁰ After adjustment for tophi (β 0.91, 95% CI -0.07, 1.90), SUA (β 0.83, 95% CI -0.66, 2.33) and dose of allopurinol (β 0.81, 95% CI -0.45, 2.07) neighbourhood deprivation was not associated with PF-10

7.6.2 The HAQ-DI

HRQOL measured by the HAQ-DI was associated with the following gout characteristics in the univariate analysis (see Table 7-4): frequency of attacks over the past 12 months, current attack of gout, a history of oligo or polyarticular attacks, treatment with allopurinol, the dose of allopurinol and the presence of tophi. After adjustments for other gout, co-morbid and socio-demographic characteristics, frequency of attacks, a history of oligo or polyarticular attacks, and treatment with allopurinol remained independently associated with HRQOL in the HAQ-DI (reduced strength of association). No association was seen between HRQOL and disease duration or SUA in the univariate or multivariate analyses.

The following co-morbid conditions were associated with HRQOL in the HAQ-DI in the univariate analysis (see Table 7-4): diabetes, stroke, hypertension, hyperlipidaemia, renal failure, myocardial infarction, angina, generalised body pain, anxiety and depression. After adjustments for other co-morbid, socio-demographic and gout characteristics, only diabetes, stroke, angina, renal failure, generalised body pain and depression remained independently associated with HRQOL. The strength of the association between HRQOL and these explanatory variables was however reduced. No associations were seen between HRQOL and TIA or renal calculi in the univariate or multivariate analyses.

The following socio-demographic characteristics were associated with HRQOL measured by the HAQ-DI in the univariate analysis (see Table 7-4): increasing age, female gender, neighbourhood deprivation, increase in BMI, lack of further education and less frequent alcohol consumption. After adjustments for other socio-demographic, co-morbid and gout characteristics in the multivariate analysis, only age, gender and less frequent alcohol consumption remained

independently associated with HRQOL. The strength of association between HRQOL and age did not alter whereas it was reduced for gender and frequency of alcohol consumption.

Table 7-4: The association of HRQOL in the HAQ-DI with gout, co-morbid and socio-demographic characteristics

	Unadjusted β (95% CI)	Residual n	Adjusted β^{31} (95% CI)	Residual n
Gout characteristics				
Frequency of attack	0.09 (0.06, 0.11)	1087	0.02 (0.00, 0.05)	667
Current gout attack	-0.40 (-0.53, -0.27)	1099	-0.04 (-0.16, 0.08)	667
Oligo-polyarticular attacks	-0.29 (-0.37, -0.20)	1096	-0.09 (-0.16, -0.01)	667
Treatment with allopurinol	-0.12 (-0.20, -0.03)	1085	-0.09 (-0.16, -0.01)	667
Dose of allopurinol	-0.19 (-0.30, -0.08)	583	-0.03 (-0.13, 0.07)	401
Tophi	0.30 (0.02, 0.59)	1028	0.19 (-0.05, 0.43)	700
Disease duration	0.02 (-0.02, 0.05)	1139	0.00 (-0.03, 0.03)	667
Serum uric acid	-0.04 (-0.20, 0.11)	447	0.04 (-0.09, 0.18)	305
Co-morbid characteristics			Adjusted β^{32} (95% CI)	
Diabetes	0.35 (0.24, 0.46)	1142	0.10 (0.00, 0.20)	725
Stroke	0.53 (0.29, 0.76)	1142	0.26 (0.06, 0.47)	
Hypertension	0.21 (0.13, 0.30)	1142	-0.04 (-0.12, 0.04)	
TIA	-0.03 (-0.22, 0.16)	1142	-0.15 (-0.32, 0.01)	
Hyperlipidaemia	0.09 (0.01, 0.17)	1142	-0.02 (-0.09, 0.06)	
Kidney failure	0.56 (0.37, 0.75)	1142	0.20 (0.03, 0.36)	
MI	0.30 (0.17, 0.44)	1142	0.05 (-0.07, 0.18)	
Kidney stones	0.15 (-0.02, 0.31)	1142	0.02 (-0.12, 0.16)	
Angina	0.42 (0.29, 0.54)	1142	0.11 (0.00, 0.23)	
Body pain	-0.45 (-0.54, 0.36)	938	-0.20 (-0.28, -0.12)	
Anxiety	0.34 (0.29, 0.39)	1067	0.00 (-0.07, 0.07)	

³¹ Adjusted for socio-demographic and co-morbid characteristics.³² Adjusted for gout (except SUA, tophi and dose of allopurinol) and socio-demographic characteristics

	Unadjusted β (95% CI)	Residual n	Adjusted β^{31} (95% CI)	Residual n
Depression	0.38 (0.34, 0.42)	1016	0.30 (0.24, 0.36)	
Socio-demographic characteristics			Adjusted β^{33} (95% CI)	
Age	0.28 (0.22, 0.34)	1142	0.27 (0.21, 0.33)	725
Gender	0.54 (0.43, 0.64)	1142	0.28 (0.18, 0.39)	
Neighbourhood deprivation	-0.08 (-0.11, -0.05)	1142	-0.02 (-0.05, 0.00)	
Ethnicity	0.04 (-0.15, 0.22)	1142	0.00 (-0.16, 0.16)	
BMI	0.12 (0.06, 0.17)	1084	0.06 (0.02, 0.11) ³⁴	
Further education	0.21 (0.10, 0.31)	1085	0.02 (-0.07, 0.11)	
Alcohol frequency	0.15 (0.13, 0.17)	1130	0.06 (0.04, 0.08)	
Relationship status	-0.08 (-0.18, 0.02)	1142	-0.05 (-0.14, 0.04)	

Abbreviations: CI: Confidence Interval; TIA: Transient Ischaemic Attack; MI: Myocardial Infarction; BMI: Body Mass Index

³³ Adjusted for gout (except SUA, tophi and dose of allopurinol) and co-morbid characteristics

³⁴ After adjustment for dose of allopurinol, BMI was no longer associated with HAQ-DI (β .05, 95% CI -0.03, 0.12)

7.6.3 The GIS

7.6.3.1 Concern overall

HRQOL measured using the concern overall (CO) sub-scale of the GIS was associated with the following gout characteristics in the univariate analysis (see Table 7-5): frequency of attacks over the past 12 months, current attack of gout, a history of oligo or polyarticular attacks, disease duration and SUA. After adjustments for other gout, co-morbid and socio-demographic characteristics in the multivariate analysis, frequency of attacks, currently having an attack of gout, history of oligo or polyarticular attacks, and SUA remained independently associated with HRQOL in the CO subscale but not disease duration. The strength of significant associations was however reduced in the multivariate analysis. No association was seen between HRQOL in the CO subscale and treatment with or dose of allopurinol or tophi in the univariate or multivariate analyses.

The following co-morbid characteristics were associated with HRQOL measured using CO in the univariate analysis (see Table 7-5): hypertension, TIA, renal failure, generalised body pain, anxiety and depression. After adjustments for other co-morbid, socio-demographic and gout characteristics in the multivariate analysis generalised body pain and depression remained independently associated with HRQOL (reduced strength of association).

The following socio-demographic characteristics were associated with HRQOL measured using CO in the univariate analysis (see Table 7-5): increasing age, neighbourhood deprivation, non-Caucasian ethnicity, higher BMI, less frequent alcohol consumption and relationship status. After adjustments for other socio-demographic, gout and co-morbid characteristics only age remained independently associated with HRQOL.

7.6.3.2 Medication side-effects

HRQOL measured using the medication side-effects (MSE) subscale was associated with the following gout characteristics in the univariate analysis (see Table 7-5): frequency of attack over the past 12 months, current attack of gout, a history of oligo or polyarticular attacks, and disease duration. After adjustments for other gout, co-morbid and socio-demographic characteristics, frequency of attack, currently having an attack of gout and history of oligo or polyarticular attacks remained independently associated with HRQOL in the MSE subscale but not disease duration. The strength of the significant associations however was reduced in the multivariate analysis. No association was seen between HRQOL in MSE and treatment with allopurinol or its dose, presence of tophi and SUA in the univariate or multivariate analyses.

HRQOL measured using MSE was associated with diabetes (protective effect), renal calculi, generalised body pain, anxiety and depression in the univariate analysis (see Table 7-5). After adjustments for other co-morbid, socio-demographic and gout characteristics only generalised body pain remained independently associated with HRQOL in MSE. No associations were seen between the HRQOL in MSE and the other co-morbid conditions in the univariate or multivariate analyses.

Increasing age, neighbourhood deprivation, non-Caucasian ethnicity, higher BMI, lack of further education, less frequent alcohol consumption and relationship status were associated with HRQOL in MSE in the univariate analysis (see Table 7-5). After adjustments for other socio-demographic, gout and co-morbid characteristics, only age remained independently associated with HRQOL in MSE (reduced strength of association). No associations were seen between HRQOL and gender in the univariate or multivariate analyses.

7.6.3.3 Unmet treatment need

HRQOL measured using the unmet treatment need (UTN) subscale of the GIS was associated with the following gout characteristics in the univariate analysis (see Table 7-5): frequency of attack over the preceding 12 months, having a current attack of gout, treatment with and the dose of allopurinol, disease duration and SUA. After adjustments for other gout, co-morbid and socio-demographic characteristics, these characteristics except the dose of allopurinol and disease duration remained independently associated with HRQOL in UTN. The strength of association between HRQOL in UTN and these variables was reduced with the exception of SUA, which had a stronger association with HRQOL in the multivariate analysis. No association was seen between HRQOL in UTN and a history of oligo or polyarticular attacks or tophi in the univariate or multivariate analyses.

In the univariate analysis, HRQOL measured using UTN was associated with the following co-morbid characteristics (see Table 7-5): generalised body pain, anxiety and depression. After adjustments for other co-morbid, gout and socio-demographic characteristics however, none of these remained independently associated with HRQOL in UTN. All other co-morbid conditions had no association with HRQOL in UTN in the univariate or multivariate analyses.

The following socio-demographic characteristics were associated with HRQOL in UTN in the univariate analysis (see Table 7-5): female gender, neighbourhood deprivation, lack of further education and less frequent alcohol intake. After adjustments for other socio-demographic, gout and co-morbid characteristics however, only frequency of alcohol consumption was independently associated with HRQOL in UTN. No association was seen between HRQOL in UTN and age, ethnicity, BMI or relationship status in the univariate or multivariate analyses.

7.6.3.4 Well-being during attack

HRQOL measured using the well-being during attack (WBDA) subscale of the GIS was associated with the following gout characteristics in the univariate analysis (see Table 7-5): frequency of attacks over the preceding 12 months, having a current attack of gout, a history of oligo or polyarticular attacks and treatment with allopurinol. After adjustments for other gout, co-morbid and socio-demographic characteristics only a history of oligo or polyarticular attacks and treatment with allopurinol remained independently associated with HRQOL in WBDA. The strength of association between HRQOL and these two gout characteristics was reduced in the multivariate analysis. There was no association between HRQOL in WBDA and the dose of allopurinol, tophi, disease duration or SUA in the univariate or multivariate analyses.

HRQOL measured using WBDA was associated with TIA, generalised body pain, anxiety and depression in the univariate analysis (see Table 7-5). After adjustments for other co-morbid, gout and socio-demographic characteristics, only depression remained independently associated with HRQOL in WBDA (strength of association reduced). There were no associations between HRQOL and any other co-morbid conditions in the univariate or multivariate analyses.

The following socio-demographic characteristics were associated with HRQOL measured using WBDA in the univariate analysis: age, neighbourhood deprivation, ethnicity, BMI, frequency of alcohol consumption and relationship status. After adjustments for other socio-demographic, gout and co-morbid characteristics, only age remained independently associated with HRQOL in WBDA (reduced strength of association). No association was seen between HRQOL and gender or further education in the univariate or multivariate analyses.

7.6.3.5 Concern during attack

HRQOL measured using the concern during attack (CDA) subscale of the GIS was associated with the following gout characteristics in the univariate analysis (see Table 7-5): frequency of attacks over the preceding 12 months, currently having an attack of gout and a history of oligo or polyarticular attacks. After adjustments for other gout, co-morbid and socio-demographic characteristics, frequency of attacks and a history of oligo or polyarticular attacks remained independently associated with HRQOL in CDA but not currently having an attack of gout. There was no association between HRQOL in CDA and treatment with or dose of allopurinol, tophi, disease duration or SUA in the univariate or multivariate analyses.

The following co-morbid characteristics were associated with HRQOL measured using the CDA subscale in the univariate analysis (see Table 7-5): generalised body pain, anxiety and depression. After adjustments for other co-morbid, gout and socio-demographic characteristics, only anxiety remained independently associated with HRQOL in CDA. Other co-morbid conditions were not associated with HRQOL in the univariate or multivariate analyses.

HRQOL measured using the CDA subscale was associated with age, neighbourhood deprivation, ethnicity, BMI, further education, frequency of alcohol consumption and relationship status in the univariate analysis but not with gender. After adjustments for other socio-demographic, gout and co-morbid characteristics, none of the socio-demographic characteristics were independently associated with HRQOL.

Table 7-5: Association of HRQOL in the GIS with gout, co-morbid and socio-demographic characteristics

	GIS CO		GIS MSE		GIS UTN		GIS WBDA		GIS CDA	
	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)
Gout characteristics³⁵										
Frequency of attack	8.45 (7.60, 9.29)	6.11 (5.00, 7.21)	4.71 (3.83, 5.59)	2.06 (0.91, 3.20)	4.17 (3.49, 4.85)	2.64 (1.75, 3.52)	2.84 (1.94, 3.74)	0.60 (-0.52, 1.73)	4.33 (3.52, 5.13)	2.48 (1.45, 3.51)
Current gout attack	-26.05 (-31.04, -21.06)	-6.66 (-12.11, -1.22)	-17.40 (-22.18, -12.62)	-6.03 (-11.66, -0.39)	-18.43 (-22.13, -14.74)	-10.61 (-14.97, -6.25)	-6.95 (-11.79, -2.10)	3.14 (-2.40, 8.67)	-11.69 (-16.14, -7.24)	1.00 (-4.09, 6.10)
Oligo-polyarticular attacks	-15.96 (-19.27, -12.64)	-5.94 (-9.42, -2.46)	-13.83 (-16.95, -10.71)	-7.60 (-11.20, -4.00)	-2.16 (-4.71, 0.38)	1.37 (-1.41, 4.15)	-14.17 (-17.26, -11.07)	-8.90 (-12.44, -5.37)	-11.10 (-14.00, -8.20)	-4.16 (-7.41, -0.91)
Treatment with allopurinol	2.60 (-0.80, 6.00)	-0.05 (-3.41, 3.31)	-0.19 (-3.38, 2.99)	-0.69 (-4.16, 2.78)	11.44 (9.02, 13.85)	9.95 (7.26, 12.64)	-5.06 (-8.22, -1.91)	-4.51 (-7.92, -1.09)	-2.41 (-5.34, 0.52)	-2.83 (-5.97, 0.31)
Dose of allopurinol	-0.50 (-4.85, 3.84)	0.16 (-4.27, 4.60)	1.77 (-2.11, 5.64)	2.06 (-2.08, 6.20)	-3.51 (-6.44, -0.58)	-2.71 (-5.98, 0.57)	0.39 (-3.55, 4.34)	0.35 (-3.79, 4.48)	-2.26 (-5.99, 1.47)	-1.82 (-5.67, 2.03)

³⁵ Adjustments made for socio-demographic and co-morbid conditions

	GIS CO		GIS MSE		GIS UTN		GIS WBDA		GIS CDA	
	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)
Tophi	-3.04 (-14.42, 8.34)	-1.55 (-13.57, 10.48)	6.14 (-4.43, 16.72)	8.20 (-3.20, 19.60)	5.51 (-2.78, 13.81)	4.15 (-5.14, 13.45)	-4.63 (-15.11, 5.86)	0.38 (-10.67, 11.42)	-0.44 (-10.19, 9.30)	2.79 (-7.37, 12.95)
Disease duration	-2.24 (-3.65, -0.83)	-0.77 (-2.20, 0.67)	-1.46 (-2.78, - 0.13)	-1.10 (-2.59, 0.38)	-2.21 (-3.25, - 1.17)	-0.28 (-1.43, 0.86)	-0.53 (-1.85, 0.79)	-1.12 (-2.58, 0.33)	-0.49 (-1.72, 0.73)	-0.42 (-1.76, 0.93)
Serum uric acid	9.30 (3.37, 15.23)	9.62 (3.10, 16.14)	2.38 (-3.51, 8.28)	1.64 (-4.84, 8.12)	5.41 (0.85, 9.97)	6.00 (0.87, 11.12)	4.06 (-1.68, 9.80)	3.32 (-2.98, 9.62)	4.02 (-1.37, 9.41)	4.49 (-1.20, 10.18)
Co-morbid characteristics³⁶										
Diabetes	-3.22 (-7.56, 1.12)	-2.10 (-6.41, 2.21)	-4.25 (-8.31, - 0.20)	-4.76 (-9.22, - 0.31) ³⁷	0.75 (-2.45, 3.96)	1.45 (-1.99, 4.90)	-0.57 (-4.61, 3.47)	-0.85 (-5.23, 3.52)	0.15 (-3.59, 3.89)	-1.91 (-5.93, 2.12)
Stroke	-2.84 (-12.28, 6.60)	-3.41 (-12.68, 5.87)	-4.83 (-13.67, 4.00)	-5.95 (-15.54, 3.63)	-4.15 (-11.11, 2.82)	-4.08 (-11.49, 3.33)	-6.42 (-15.19, 2.36)	-9.38 (-18.79, 0.03)	-0.25 (-8.39, 7.89)	-4.33 (-12.99, 4.33)
Hypertension	-3.91 (-7.29, -0.54)	-2.85 (-6.41, 0.71)	-1.09 (-4.25, 2.08)	-0.06 (-3.74, 3.62)	-0.41 (-2.91, 2.09)	0.14 (-2.71, 2.99)	-1.63 (-4.78, 1.52)	-0.33 (-3.95, 3.29)	-0.01 (-2.93, 2.90)	-0.88 (-4.21, 2.45)

³⁶ Adjusted for gout (except SUA, tophi and dose of allopurinol) and socio-demographic characteristics

³⁷ Diabetes was not associated with MSE after adjusting for SUA (β -8.22, 95% CI -17.04, 0.61) or allopurinol dose (β -3.77, 95% CI -9.37, 1.83)

	GIS CO		GIS MSE		GIS UTN		GIS WBDA		GIS CDA	
	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)
TIA	-8.65 (-16.01, -1.29)	-4.35 (-11.62, 2.91)	-5.13 (-12.02, 1.77)	-1.85 (-9.36, 5.66)	-4.17 (-9.61, 1.27)	-2.14 (-7.94, 3.67)	-7.71 (-14.56, -0.86)	-3.56 (-10.93, 3.81)	-4.26 (-10.61, 2.10)	-1.37 (-8.16, 5.41)
Hyperlipidaemia	-0.49 (-3.81, 2.83)	1.72 (-1.67, 5.10)	0.07 (-3.04, 3.18)	1.06 (-2.44, 4.56)	-0.36 (-2.81, 2.09)	-0.35 (-3.06, 2.36)	-0.22 (-3.31, 2.87)	1.33 (-2.11, 4.77)	0.90 (-1.96, 3.77)	1.20 (-1.96, 4.37)
Kidney failure	10.43 (2.72, 18.15)	5.55 (-1.92, 13.01)	5.35 (-1.89, 12.58)	1.95 (-5.76, 9.66)	-0.23 (-5.94, 5.49)	-2.81 (-8.77, 3.16)	5.14 (-2.06, 12.33)	0.75 (-6.83, 8.32)	5.87 (-0.79, 12.54)	0.24 (-6.73, 7.21)
MI	-2.90 (-8.37, 2.56)	-1.74 (-7.32, 3.83)	0.27 (-4.84, 5.38)	0.90 (-4.86, 6.66)	1.02 (-3.02, 5.05)	0.24 (-4.21, 4.69)	-1.35 (-6.43, 3.74)	-0.25 (-5.91, 5.40)	1.64 (-3.07, 6.35)	0.22 (-4.98, 5.42)
Kidney stones	5.24 (-1.27, 11.74)	-0.04 (-6.29, 6.21)	7.90 (1.82, 13.97)	4.15 (-2.30, 10.61)	2.60 (-2.20, 7.41)	1.97 (-3.02, 6.96)	-1.09 (-7.14, 4.97)	-5.56 (-11.90, 0.78)	4.73 (-0.88, 10.33)	0.10 (-5.73, 5.93)
Angina	-1.49 (-6.47, 3.50)	-2.41 (-7.51, 2.70)	-0.24 (-4.90, 4.42)	-2.63 (-7.90, 2.64)	1.73 (-1.95, 5.41)	0.45 (-3.63, 4.52)	1.70 (-2.93, 6.34)	-0.03 (-5.21, 5.15)	3.40 (-0.89, 7.69)	0.14 (-4.63, 4.90)
Body pain	-16.02 (-19.75, -12.29)	-6.75 (-10.27, -3.23)	-12.17 (-15.70, -8.64)	-6.17 (-9.81, -2.54)	-6.58 (-9.40, -3.76)	-2.11 (-4.92, 0.70)	-12.99 (-16.50, -9.49)	-8.62 (-12.19, -5.05) ³⁸	-10.98 (-14.23, -7.73)	-3.92 (-7.20, -0.64)

³⁸ After adjusting for SUA, body pain was not associated with WBDA (β -2.93, 95% CI -8.87, 3.00) or CDA (β -2.49, 95% CI -7.84, 2.87)

	GIS CO		GIS MSE		GIS UTN		GIS WBDA		GIS CDA	
	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)
Anxiety	9.18 (7.04, 11.31)	1.44 (-1.59, 4.48)	8.48 (6.49, 10.48)	2.63 (-0.50, 5.77)	3.18 (1.57, 4.79)	-0.88 (-3.30, 1.55)	9.44 (7.47, 11.41)	1.24 (-1.84, 4.32)	11.27 (9.50, 13.04)	4.13 (1.30, 6.96)
Depression	7.82 (6.05, 9.59)	2.57 (0.02, 5.12)	6.98 (5.32, 8.63)	2.61 (-0.03, 5.24)	3.31 (1.98, 4.64)	1.92 (-0.12, 3.96)	8.90 (7.29, 10.51)	5.89 (3.30, 8.48)	9.46 (7.99, 10.92)	4.71 (2.33, 7.09) ³⁹
Socio-demographic characteristics⁴⁰										
Age	-10.17 (-12.54, -7.80)	-6.87 (-9.56, -4.17)	-7.03 (-9.28, -4.78)	-4.25 (-7.03, -1.46)	-0.81 (-2.61, 1.00)	-0.47 (-2.62, 1.68)	-10.35 (-12.54, -8.15)	-8.03 (-10.76, -5.30)	-5.67 (-7.75, -3.59)	-3.11 (-5.62, -.59) ⁴¹
Gender	1.13 (-3.31, 5.57)	1.03 (-3.64, 5.70)	-1.53 (-5.68, 2.62)	-2.43 (-7.25, 2.39)	3.77 (0.50, 7.04)	0.50 (-3.23, 4.22)	-3.84 (-7.96, 0.29)	-3.53 (-8.27, 1.20)	0.36 (-3.46, 4.19)	-0.11 (-4.47, 4.25)
Neighbourhood deprivation	-2.34 (-3.50, -1.18)	-0.53 (-1.66, 0.60)	-1.46 (-2.55, -0.36)	-0.01 (-1.18, 1.15)	-0.93 (-1.80, -0.07)	-0.08 (-0.98, 0.83)	-1.32 (-2.41, -0.24)	0.16 (-0.99, 1.30)	-2.40 (-3.40, -1.40)	-0.80 (-1.86, 0.26)

³⁹ After adjusting for dose of allopurinol, the association between depression and CDA was not statistically significant (β 2.10, 95% CI -1.19, 5.40)

⁴⁰ Adjusted for gout (except SUA, tophi and dose of allopurinol) and co-morbid characteristics

⁴¹ After adjustment for SUA, age was not associated with CDA (β -2.62, 95% CI -6.75, 1.50)

	GIS CO		GIS MSE		GIS UTN		GIS WBDA		GIS CDA	
	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)	Unadjusted β (95% CI)	Adjusted β (95% CI)
Ethnicity ⁴²	13.66 (6.28, 21.04)	4.83 (-2.38, 12.05)	15.66 (8.77, 22.54)	10.17 (2.71, 17.63)	3.73 (-1.75, 9.21)	0.63 (-5.13, 6.40)	13.52 (6.66, 20.38)	7.54 (0.22, 14.87)	15.60 (9.27, 21.94)	9.97 (3.24, 16.71)
BMI	3.36 (1.11, 5.61)	-0.05 (-2.20, 2.11)	2.26 (0.15, 4.37)	-0.08 (-2.30, 2.15)	0.15 (-1.52, 1.81)	-0.66 (-2.38, 1.06)	2.90 (0.80, 5.00)	-0.20 (-2.38, 1.99)	2.89 (0.95, 4.83)	0.48 (-1.54, 2.49)
Further education	3.08 (-0.98, 7.13)	-1.01 (-4.86, 2.84)	3.92 (0.13, 7.71)	1.94 (-2.04, 5.91)	3.78 (0.78, 6.77)	1.06 (-2.02, 4.13)	2.87 (-0.90, 6.65)	1.60 (-2.31, 5.50)	4.79 (1.30, 8.28)	2.09 (-1.50, 5.68)
Alcohol frequency	1.64 (0.63, 2.65)	0.55 (-0.50, 0.59)	1.30 (0.35, 2.24)	0.52 (-0.56, 1.60)	1.80 (1.06, 2.54)	1.11 (0.27, 1.94)	1.16 (0.22, 2.10)	0.56 (-0.50, 1.62)	1.64 (0.77, 2.51)	0.38 (-0.59, 1.36)
Relationship status	4.10 (0.15, 8.04)	-0.09 (-3.97, 3.80)	3.74 (0.05, 7.43)	1.24 (-2.77, 5.25)	-0.04 (-2.96, 2.88)	0.10 (-3.00, 3.20)	5.97 (2.31, 9.63)	1.15 (-2.79, 5.09)	4.00 (0.60, 7.40)	0.98 (-2.64, 4.61)

Abbreviations: GIS: Gout Impact Scale; CO: Concern Overall; MSE: Medication Side Effects; UTN: Unmet Treatment Need; WBDA: Wellbeing during attack; CDA: Concern During Attack; CI: Confidence Interval; TIA: Transient Ischaemic Attack; MI: Myocardial Infarction; BMI: Body Mass Index.

⁴² After adjusting for tophi, ethnicity was not associated with WBDA (β 7.31, 95% CI -1.15, 15.76), MSE (β 7.96, 95% CI -0.77, 16.69). After adjusting for SUA, ethnicity was not associated with CDA (β 8.47, 95% CI -3.16, 20.09). After adjusting for dose of allopurinol, ethnicity was not associated with MSE (β 7.61, 95% CI -3.07, 18.30), WBDA (β 6.88, 95% CI -3.80, 17.55), CDA (β 3.57, 95% CI -6.37, 13.51).

7.7 Discussion

Poor HRQOL (measured by the GIS) was associated with frequency of attacks over the preceding 12 months, currently having an attack of gout, a history of oligo or polyarticular attacks, SUA and treatment with allopurinol. Although treatment with allopurinol was associated with reduced unmet treatment need, it was associated with higher concerns about well-being during an acute attack and greater disability in the HAQ-DI. Poor generic HRQOL (PF-10 and HAQ-DI) was associated with frequency of attacks, oligo or polyarticular attacks and treatment with allopurinol.

In the unadjusted analyses, paradoxical statistically significant associations were seen between better HRQOL in the GIS and:

- The presence of diabetes mellitus (lesser self-reported medication side-effects)
- Hypertension (lesser gout concern overall)
- TIA (lesser concern overall for gout and concerns regarding well-being)

These associations were however not significant in the multivariate adjusted analysis. In the adjusted analyses, the generic questionnaires were associated with physical co-morbidities such as stroke, angina, diabetes, renal failure, generalised body pain as well as psychological co-morbidities such as depression. The GIS however was associated with psychological co-morbidities (anxiety and depression) and generalised body pain but not co-morbid medical conditions.

HRQOL measured by the PF-10 and HAQ-DI was independently associated with age and female gender independent of other socio-demographic, co-morbid and gout characteristics. Poor HRQOL measured by the GIS and generic measures was associated with decreasing frequency of alcohol consumption independent of other characteristics. In contrast to the generic

questionnaires, better HRQOL (lower concerns about side-effects and lower overall gout concern) in the GIS was reported by older participants compared to younger ones.

In addition to demonstrating clear association of HRQOL with markers of gout severity (frequency of attacks, history of oligo or polyarticular attacks, SUA > 360 $\mu\text{mol/L}$), there were some unexpected findings in this study. Despite being associated with reduced unmet treatment need, treatment with allopurinol was also associated with greater concerns for well being during an acute attack and greater disability. The WBDA sub-scale focuses on work, recreational activities, mood, sleep, mobility and self-care (Hirsch, Lee et al. 2008). It is plausible that those being treated with allopurinol are perceived to have more severe gout than those untreated and find it difficult to do activities relevant to the WBDA sub-scale. The unexpected association between better HRQOL and diabetes may be due to participants with diabetes having regular medical checks (surveillance bias (Schlesselman, Schneiderman 1982)) and are therefore more likely to be diagnosed with gout and treated with allopurinol. Lesser medication side effects may result from regular monitoring and reduction of SUA by titrating the dose of allopurinol and counselling by healthcare professionals. Other plausible explanations could be diabetes having a protective effect on the development of gout through the uricosuric effects of glycosuria (Rodríguez, Soriano et al. 2010) and the impaired inflammatory state seen in diabetes (Choi, Mount et al. 2005).

The association of poor HRQOL in the generic questionnaires with female gender is plausible as females with gout are more likely than men to be older, be prescribed diuretics, have tophaceous and polyarticular gout (including upper limb involvement) (Dirken-Heukensfeldt, Teunissen et al. 2010). In a population based study, females with gout were shown to be more likely than men to have co-morbidities such as dyslipidaemia, hypertension, cardiovascular and peripheral vascular disease and renal impairment (Harrold, Yood et al. 2006). Better HRQOL in those who reported

alcohol consumption compared to those who were teetotal in this study may be explained by moderate alcohol intake acting as a protective factor for improved health in those with and without chronic musculoskeletal pain (Arvidsson, Arvidsson et al. 2008). Low to moderate alcohol intake was also associated with a reduction in fibromyalgia symptoms and improvement in HRQOL (Kim, Vincent et al. 2013). It is possible that alcohol acts as an agonist of γ - amino butyric acid (GABA) which is found to be low in patients with fibromyalgia (Kim, Vincent et al. 2013). Increase in GABA may alter pain perception in fibromyalgia and possibly in other chronic pain conditions such as gout. Moderate alcohol intake is also associated with lesser risk of developing rheumatoid arthritis and halting disease progression through reduction in the pro-inflammatory cytokines (Maxwell, Gowers et al. 2010). Alcohol may also be seen as a stress reliever and promote social integration, both of which may be associated with a better HRQOL (Kim, Vincent et al. 2013).

Finally, neither the generic questionnaires nor the GIS were associated with the dose of allopurinol or disease duration in the adjusted analyses. Lack of association with the dose of allopurinol may be secondary to inadequate dose titration to achieve the target SUA of ≤ 360 $\mu\text{mol/L}$ in this study (median dose of 300 mg per day and 97% of those with a SUA > 360 $\mu\text{mol/L}$ still receiving ≤ 300 mg allopurinol). Participants may be unaware of the need for titration of the dose of allopurinol and subsequently may not perceive it as an important determinant of quality of life, as elicited in the nested qualitative interviews (chapter 8). It is likely that those with longer disease durations are likely to be older. Worse HRQOL is more likely in those who are older due to increase in frailty, multiple co-morbidities and polypharmacy (Nobili, Garattini et al. 2011).

7.7.1 Comparison with existing studies

The association of HRQOL with allopurinol and SUA are novel findings when compared to previous another UK based primary care study of HRQOL in gout (Roddy, Zhang et al. 2007c). HRQOL measured using the WHO-QOL BREF was not associated with treatment with allopurinol or SUA (Roddy, Zhang et al. 2007c). This study however recruited from two UK general practices only, had a lower response rate (23%) compared to our study (65.5%) and used the generic WHO-QOL BREF (instead of the GIS in our study) to ascertain HRQOL. The self-reported diagnosis of gout was validated by a physician and SUA was measured at the time of the clinical assessment, unlike our study.

The association of GIS with SUA in this study is different from the minimal correlation ($r < 0.29$) between SUA and GIS found in a USA primary and secondary care based multicentre study (Hirsch, Terkeltaub et al. 2010). Although the ascertainment of SUA has not been contemporaneous in either study, the US based study recorded the most recent SUA (validated by a physician) in contrast to the highest SUA in the preceding 2 years in this study.

Similar to this study findings, HRQOL measured by generic questionnaires such as the Short Form (SF) 12 and SF-6D and the GIS have previously been associated with frequency of attacks (Khanna, Nuki et al. 2012; Hirsch, Lee et al. 2008). Although currently having an attack of gout was associated with HRQOL measured by some sub-scales of the GIS in this study, no association was seen with the acute attack sub-scales of the GIS in the multivariate adjusted analysis. This was an unexpected finding as the 'during attack' sub-scales would likely be preferentially related to a 'within attack experience' (Hirsch, Lee et al. 2008). A US based cross-sectional study has shown moderate to large correlations between pain during a typical attack and gout concern overall, concern and well being during attack sub-scales (Hirsch, Terkeltaub et al. 2010). This however

was a multicentre study recruiting from both primary and secondary care settings with validation of self-reported gout characteristics from physicians.

The lack of association between HRQOL measured by the GIS and tophi in this study is reflected in the previously demonstrated minimal correlation between patient-rated severity of gout and tophi (Sarkin, Levack et al. 2010). Although an important objective measure of assessment of gout from a physician's perspective, tophi may not be perceived as causing hindrance to daily activities and quality of life by patients (Sarkin, Levack et al. 2010). However disability and HRQOL in generic questionnaires (HAQ, SF-12v2, SF-6D and SF-36) have previously been associated with tophi (Alvarez-Nemegyei, Cen-Piste et al. 2005; Khanna, Nuki et al. 2012; Sundy, Schumacher et al. 2006), a finding not replicated in this study. These studies have different methods of data ascertainment (self-reported tophi (Khanna, Nuki et al. 2012), gout diagnosed by Wallace criteria (Alvarez-Nemegyei, Cen-Piste et al. 2005)) and measurement of HRQOL (SF-12 (Khanna, Nuki et al. 2012), Spanish HAQ (Alvarez-Nemegyei, Cen-Piste et al. 2005)), a more selective source of recruitment (National health and wellness survey, Lightspeed research panel (Khanna, Nuki et al. 2012) and secondary care clinics (Alvarez-Nemegyei, Cen-Piste et al. 2005)) and participants with different severity of gout compared to this study. The differences in findings may also be explained by the low reported presence of tophi (2.3%) in this study. Also the presence of tophi was ascertained from medical records up to 2 years preceding the study and would not necessarily be contemporaneous with patient-reported questionnaire data. It is plausible that the association of tophi with HRQOL may be indirectly mediated by other markers of disease severity (frequency of attack, SUA, history of oligo or polyarticular attacks) in this study.

Co-morbidities such as renal disease, cardiovascular disease and diabetes have independently been associated with physical more than psychological SF-36 HRQOL in gout previously (Lee,

Hirsch et al. 2009; Singh, Strand 2008). The impact of gout on psychosocial well being has been illustrated previously in a qualitative study of the experience of living with gout (Lindsay, Gow et al. 2011). None of these studies however ascertained the prevalence (or impact) of anxiety or depression in those with gout. The independent association of anxiety and depression with HRQOL in gout has only been shown in this study. This may be explained by the significant prevalence of depression in gout of 13.5% (measured using the PHQ-9 in the National Health and nutrition examination survey 2009-2010 to 20%) (Ege, Messias et al. 2013) and anxiety 6% (measured using the hospital anxiety and depression scale in a Singaporean secondary care cross-sectional study of 50 patients with gout) (Mak, Tang et al. 2011).

Comparable to the findings of this study (poor generic HRQOL but lower concerns for gout overall and treatment side-effects), poorer physical health and greater musculoskeletal disability but better vitality and mental health in older compared to younger people have been reported previously (Becker, Schumacher et al. 2009; Alvarez-Nemegyei, Cen-Piste et al. 2005).

7.7.2 Strengths of the study

This is the first UK primary care-based cross-sectional study of both generic and disease-specific HRQOL in gout in a large (1184) sample of varying disease severity. HRQOL has been comprehensively assessed using a combination of two generic (PF-10 and HAQ-DI) and a gout-specific questionnaire (GIS), which has not been done previously. Both the HAQ-DI and the SF-36 which includes the PF-10 have previously been endorsed by OMERACT as validated measures of disability and HRQOL in gout (Singh, Taylor et al. 2011). Using multidimensional composite outcome measures allows the capture of the complex impact of gout on HRQOL that differs depending on treatment type and patient characteristics (Sarkin, Gnanasakthy et al. 2013).

In addition to previously known clinical (tophi, co-morbid conditions, disease duration, alcohol intake) and biochemical (level of uric acid) indicators of disease severity (Alvarez-Nemegyei, Cense et al. 2005) other characteristics such as current attack of gout and the dose of allopurinol were also examined as possible associates of HRQOL. Multivariate linear regression adjusted for all measured confounding factors has shown independent associations of gout, co-morbid and socio-demographic characteristics of HRQOL in gout. The large sample size underpins the assumptions of normal distribution of HRQOL data.

7.7.3 Limitations of the study

SUA and tophi were ascertained at any time-point in the two years preceding the study, hence may not be contemporaneous with questionnaire completion. In such cases, there may be a false lack of association between these objective measures and HRQOL. The lack of documented tophi in the medical records was assumed equivalent of absence of tophi. It is plausible that primary care physicians may not recognise tophi, may not look for them during their clinical examination, or may not record their presence. Where SUA was not recorded, it was assumed that it was not checked, leading to high levels of missing data. Statistical analyses have been adjusted to minimise the level of missing data in regression models. Inclusion into regression models were restricted to those who consented to medical record review when examining the association of tophi with HRQOL, those with a recorded SUA when examining hyperuricaemia and those on allopurinol when examining allopurinol dose.

Severity of co-morbidities was not assessed and may have increased the strength of association had this been included (Fortin, Lapointe et al. 2004). The GIS used in this study, remains to be validated by the OMERACT group, mainly due to lack of familiarity, lack of clarity over what domains it measures and concerns about the psychometric properties of the UTN sub-scale

(Singh, Taylor et al. 2011). However the concern overall sub-scale has been endorsed as having good internal consistency, test-retest reliability (Khanna, Sarkin et al. 2011) and construct validity (Hirsch, Lee et al. 2008), which is reflected in its association with multiple gout characteristics in this study.

7.7.4 Implications for clinical practice

Self-reported and objective gout characteristics (except tophi, disease duration and dose of allopurinol) are independently associated with HRQOL in this study, implying a substantial impact of gout on HRQOL, comparable to that of other chronic conditions such as congestive heart failure (Lee, Hirsch et al. 2009). As evident from the results, patients with one or more attack per year, a history of oligo or polyarticular attacks and SUA > 360 $\mu\text{mol/L}$ have poorer HRQOL. This suggests that pharmacological urate-lowering treatment should be offered early, before the disease progresses to include these characteristics, or if already present, to prevent worsening of disease severity. The British Society of Rheumatology (BSR) guidelines (2007) recommend commencing ULT in those who have 2 or more attacks per year (Jordan, Cameron et al. 2007). European League against Rheumatism (EULAR) guidelines do not reach a consensus as to whether ULT should be started after the first attack or waiting until further attacks occur but do recommend ULT for multiple joint involvement (Zhang, Doherty et al. 2006a). Patient concerns about well being may be reduced through counselling about the indications and risk benefit profile of ULT.

Even if being treated with allopurinol, the dose was not associated with HRQOL in this study. This may be due to inadequate titration of allopurinol dose to reduce SUA < 360 $\mu\text{mol/L}$. Titration of allopurinol to reduce SUA < 360 $\mu\text{mol/L}$ has been shown to deplete urate crystals in knee synovial aspirate (Li-Yu, Clayburne et al. 2001), reduce the number and size of tophi (Perez-Ruiz, Calabozo et al. 2002b) and prevent attacks (Li-Yu, Clayburne et al. 2001) (Shoji, Yamanaka et al. 2004).

Dissolution and eventual disappearance of urate crystals (and therefore tophi) will cure gout (Zhang, Doherty et al. 2006a), therefore gout associated HRQOL should be unaffected in such cases.

In addition to gout characteristics associated with HRQOL in this study, physical and psychological co-morbid conditions also adversely affect HRQOL. Screening for co-morbid conditions (namely hyperlipidaemia, hypertension, diabetes, obesity) has been recommended by existing EULAR (Zhang, Doherty et al. 2006a) and ACR guidelines (Khanna, Fitzgerald et al. 2012). Patient and physician awareness of co-morbidities associated with gout and their treatment alongside gout may prevent worsening of HRQOL by reducing SUA (Zhang, Doherty et al. 2006a). A double blind placebo controlled trial (Bastow, Durrington et al. 1988) and an open cross-over study (Feher, Hepburn et al. 2003) have shown that in addition to reducing lipid level, fenofibrate reduced SUA. Similarly losartan was effective in reducing SUA in addition to blood pressure in a randomised double blind cross-over study (Würzner, Gerster et al. 2001). However none of the existing guidelines recommend screening for or treating psychological co-morbidities in gout, which are also associated with poor HRQOL as seen in this study.

7.7.5 Implications for further research

Cross-sectional associates of HRQOL could be explored further to examine which specific characteristics influence HRQOL. For example, during a current attack, the duration of symptoms, pain intensity, number and site of joints involved and treatments taken may provide further information to target those at risk of poor outcome. Contemporaneous record of SUA and tophi may more accurately reflect any association (or lack of) with HRQOL but may need modification to the current study design (provision for clinical contact at the time of questionnaire completion).

Prospective follow-up will also highlight whether these associated gout characteristics predict HRQOL long-term.

Worse HRQOL in the WBDA sub-scale of the GIS was noted in those on allopurinol. Although plausible that these participants have a more severe form of gout, this needs to be investigated further. Markers of disease severity (frequency of attacks in the preceding 12 months, SUA, history of joints involved in a typical attack) in those on allopurinol could be compared to those not on allopurinol within this cross-sectional study. Further research into participants' perception of urate-lowering treatment may also shed light on why they have low unmet treatment needs yet high concerns about their well being during attacks of gout. Whether any counselling was received from healthcare physicians about the possibility of the onset of acute attack may also inform future clinical practice to improve outcome.

Although the choice of using generic or gout-specific questionnaires in future research studies will be guided by the research objectives. For example, HRQOL in the generic questionnaires was associated with some but not all gout characteristics that were detected as associates of HRQOL by the GIS. However HRQOL in the generic questionnaires was associated with medical co-morbid conditions which were not seen as associates of HRQOL in the GIS. Studies focusing on the specific impact of gout may wish to use the GIS and those evaluating the impact of gout as well as other patient characteristics may benefit from using the PF-10 and HAQ-DI. However a combination of the two may provide a comprehensive overview of the role of gout and other associated factors in HRQOL.

7.7.6 Conclusion

This chapter provides evidence that gout adversely affects HRQOL (measured by the PF-10, HAQ-DI and GIS) independent of co-morbid and socio-demographic characteristics. However co-morbid and socio-demographic characteristics still contribute to poor HRQOL in gout. Gout-specific questionnaire such as the GIS has detected an association between gout-characteristics (current attack and SUA) and HRQOL that was not seen in the generic HRQOL questionnaires. Those with patient-reported and objective associates of poor HRQOL in gout should be informed about the indications for ULT and its role in preventing progression to irreversible multi-system damage caused by gout. Co-morbid conditions should be screened for and treated alongside gout. The next chapter provides a qualitative account of participants' experiences, beliefs and attitudes towards how gout and its treatments affect their HRQOL.

8 The impact of gout and its treatments on Health Related Quality of Life (HRQOL): A qualitative study of participants' perspectives using focus group interviews

8.1 Introduction

The previous two chapters provided a quantitative description of participant characteristics (gout, co-morbid and socio-demographic) and their association with HRQOL in gout. This chapter provides a detailed qualitative interpretation of a sub-sample of participants' personal experiences of how gout and its treatments may affect HRQOL. It complements the results of the quantitative data analysis by explaining how some of the gout-specific factors previously identified affect HRQOL. It also adds to previous findings by identifying other previously unexplored factors (such as diet) that have an impact on participants' HRQOL. The aim and objective of this nested qualitative study was to gain an in-depth understanding of participants' experiences, beliefs and attitudes towards the impact of gout and its treatments on HRQOL using focus group interviews. The methods pertaining to the design, recruitment of participants, conduct and analysis of the interview data have been described in detail in chapter 4 (Study design and methods).

8.2 Results

8.2.1 Study sample

Of the 19 participants invited for the interviews, 16 attended. The wife of one participant (who acted as a carer for her husband but has not herself been diagnosed with gout) volunteered to participate in the interview, hence the total number of participants was 17 (15 males).

Participant characteristics are presented in Table 8-1. All interviews were conducted between November and December 2012. All participants provided written informed consent for their quotations to be used in any narrative account arising from the interviews.

Table 8-1: Participant characteristics

Survey ID	Male/ Female	Age (years)	Interview location GP/ K	No. of attacks in last 12 months	On allopurinol Yes=1, No=2
430	F	76	GP	5	1
452	M	75	K	5	2
686	M	73	GP	2	2
84	M	55	K	3	1
441	M	67	K	1	2
476	M	68	K	3	1
478	M	85	K	3	2
501	M	77	K	2	1
562	M	72	GP	2	1
387	M	81	K	3	1
445	M	68	K	2	1
237	M	64	K	2	2
233	M	64	K	2	1
407	M	78	K	3	1
456	M	60	K	4	2
463	M	63	K	3	1
701	M	75	K	5	2
Carer	F	unknown	K	NA	NA

Abbreviations: NA: not applicable; GP: general practice; K: Keele University; M: male; F: female; No.: number

8.2.2 Higher order themes and sub-themes

The impact of gout on HRQOL is illustrated through higher order themes (numbered sub-sections) which incorporate many sub-themes (headings in bold and italics) in the sections below.

Quotations from female participants have been marked with *F*. All unmarked quotations were from male participants.

8.2.2.1 Characteristics of gout

Pain

Pain could affect multiple sites in the body and vary in intensity, with its extreme form severe enough to make some participants cry. The duration of severe pain could last as long as 3 weeks but some participants reported a low intensity of pain lasting almost a decade of life.

“Mine lies all over my body, everywhere”

F: “It gets that painful I’ll cry. I can’t get rid of it.”

Gout caused isolation through reduced mobility arising from pain and swelling in the joints.

Reduced mobility may cause physical disability which is a key component of HRQOL in the generic questionnaires such as the HAQ-DI.

“So I can’t really go anywhere or do anything in that sense”

Being immobile and unable to do things or inability to go out of the house also led to feelings of boredom. Boredom was an example of reduced psycho-social HRQOL provided by a participant as illustrated in the quotation below and it may be at one end of a spectrum of characteristics of reduced psycho-social HRQOL such as isolation, desperation to amputate the affected limb or even suicidal tendency as described in other research (Lindsay, Gow et al. 2011).

“You’re so bored sat there not being able to move your foot, [laughter] that you get psychological side effects”.

*F: "You really bang your head against the wall and you - there isn't anything that'll take that off
for a day perhaps"*

Desperation to relieve the severe pain of gout was also apparent from some of the extreme self-management techniques described by participants. The pain of sitting in freezing cold water was deemed more bearable than the pain associated with an attack of gout for example.

"I'll get into freezing cold water and sit there. [yeah] I take that pain to take that off"

It was anticipated that pain would be worsened upon contact of the gout affected body part with another person or object during sleep, thereby reducing its quality and comfort.

*"You can't turn over, when you're half asleep, you accidentally touch something. You're frightened
that she's going to touch it"*

Gout was considered serious if larger joints were involved in an attack rather than small joints of the feet for example. This suggests that for some participants the impact of gout on HRQOL may be influenced by which joints are affected. This example illustrates the point that people with gout may attribute any pain to gout, regardless of its underlying cause.

*"I mean a toe is relatively innocuous, if you've got it in your knees or hips or something, then yeah,
it's a little more worrying".*

Gout more painful and harder to treat than other conditions

The pain in gout was considered to be of higher intensity and longer lasting than that in a fractured limb for example. Treatment of gout was also considered less effective in relieving pain when compared with the treatment of a fracture. These comments reflect the impact of gout and its treatments (or lack of) on HRQOL.

*"If it breaks, [yeah] you go to the hospital, put it in plaster, and you're - a bit of a throbbing and it's
gone, but with gout it's bang, bang, bang for days and days".*

Unpredictable nature of attacks

Although some participants described a constant level of pain, the unpredictable onset of acute attacks led to difficulties in planning activities or social engagements in the future. Participants were often fearful of making commitments which may not be fulfilled in the event of a sudden attack. Lack of social engagement due to not making or cancelling plans may affect the psychological HRQOL.

“It's the unpredictability of it, you know, you make a plan to, I don't know, maybe go to theatre in five weeks' time and when it gets closer you think god, I hope I don't get gout just the night before.”

Fear of the recurrent and unpredictable attacks of gout made one participant consider treatment with allopurinol, which he perhaps would not have considered otherwise. Although driven by fear of unpredictable attacks, seeking ULT may lead to improved longer term HRQOL through reduction in the number of attacks and preventing irreversible bone and joint damage.

“The only reason that I went back this time to - to see about it was the fact that I was a little bit frightened if I was going to go on holiday the next day it was going to clobber me that day”.

Modification in lifestyle

Symptoms (pain, swelling, unpredictable nature of attacks) of gout caused hindrance in performing activities of daily living which meant that participants made modifications in their lifestyle and work environment. Relocation to warmer climates to help reduce the symptoms was also reported. Impact of gout on multiple facets of daily life can have an effect on HRQOL.

“Well I couldn't get my shoe on, last - a week ago since my last one”

“I stopped doing these high impact erm exercises, I stopped long distance walking, because it was painful”

"I'm a long distance runner, so when I can't run like I hate it"

"Like it's office work now, like you know a desk job now"

"Because the damp weather, the cold and damp weather, is just not helping him at all. And they moved, they sold up and they moved to warmer climates"

The impact of gout symptoms on physical functioning (Lindsay, Gow et al. 2011), work absence and productivity has been seen previously (Kleinman, Brook et al. 2007).

Gout not only limited the lifestyle of those affected by it but also of family members who may care for them. Family members may feel unhappy or guilty if the person affected with gout cannot participate in activities they do, as illustrated by the quotation below from the wife (who did not have gout) of a participant with gout.

F (carer): "I could go out and leave him. [right, yeah] But there's no way I would. [okay] So it does have an effect on the whole unit"

Nevertheless the restrictions or changes in lifestyle associated with caring for someone with gout was acknowledged by her.

F (carer): "Well we can't go out and do the same things"

8.2.3 Understanding of gout

Over-indulgence as a cause for gout

Aware of the dietary causes of gout, one participant anticipated attacks of gout with what he perceived as excessive consumption of food and alcohol.

"Yeah I know I kind of guess when I might be getting one, [yeah] by the fact that I've over indulged somewhere"

The belief that dietary factors were primarily responsible for causing gout was seen in this study as well as that carried out in 142 participants using the brief illness perception questionnaire (Dalbeth, Petrie et al. 2011). Despite such beliefs, participants in that study did not perceive that gout was influenced by their personal actions. Personal control scores have been negatively associated with identity, consequences and emotional response domains of illness perception (Dalbeth, Petrie et al. 2011). By contrast participants in my study considered dietary modifications (particularly if they considered their previous dietary habits to be 'overindulgent') a key to preventing recurrent attacks. Eating cherries to prevent recurrent attacks was common practice amongst a number of participants.

"I have cherries. And I have seeds sometimes, celery seeds".

The study by Dalbeth, Petrie et al. 2011 however was not qualitative in nature and set amongst participants with disease duration of less than 10 years in New Zealand, where a significant proportion of the population are of Maori ethnicity who may have an earlier onset and a more severe form of gout (Klemp, Stansfield et al. 1997).

Gout not a disease

A recurrent emphasis from participants was placed on gout not being considered as a 'disease'. Instead they considered it to be an illness resulting from a 'natural' accumulation of metabolites in the body. Support for this health belief was sought from the other participants by asking for confirmation, as illustrated in the quotations below.

"For me, disease is something like malaria and erm... infection like, yeah. But it isn't is it, it's just a build-up of stuff that's naturally in your body"

"Is it - is it a modern - modern disease? It isn't a disease is it, is it a modern...?"

"Well, it's a condition"

The distinction between disease (a biological condition) and illness (social meaning of the condition) (Eisenberg 1977) may be rooted within social constructionism, which explains that illnesses are socially constructed at an experiential level which is based upon the individual's understanding of the disease and perceptions of his identity post diagnosis (Conrad, Barker 2010).

"Illness is a social designation, by no means given in the nature of medical fact" (Gusfield 1967, p.180)

Conditions such as gout may be embedded with cultural meaning (not necessarily related to the disease) which influence how society views those with the illness and hence shape their experience of living with it (Conrad, Barker 2010). The classification of gout as a 'disease' may be associated with negative perceptions or embarrassment in the society (as is the case in some infectious diseases such as Human Immunodeficiency Virus or Acquired Immunodeficiency Syndrome (Brown, Macintyre et al. 2003)). HRQOL is often considered "in the context of the culture or value systems individuals live in" (WHOQOL Group 1993) and is likely to be adversely affected by negative societal perceptions.

Although considered to be a widespread and serious condition, some participants felt that gout was under-reported within the community. Under-reporting of gout is associated with inadequate treatment which may lead to progressive gout (Lindsay, Gow et al. 2011) and poor HRQOL as a result.

"There's more people than what we think who get it a bit, not coming forward and saying this is a bigger serious problem"

Some were surprised when diagnosed with gout, as it was a completely unexpected diagnosis. Such feeling may arise from unawareness of gout previously but also due to reluctance to accept the diagnosis due to the stigma attached to the societal image of who typically gets affected by gout. Stereotypical ideas of gout affecting those who could afford luxurious food and drink (such

as meat and alcohol, traditionally associated with wealth and unhealthy lifestyle) were still widely prevalent in society according to participants.

“It’s this thing ...they don’t realise what it is and they just use the old wives’ tale, the port and pheasant, rich living”

Participants may not consider themselves akin to the stereotypical media portrayal of those who get gout (wealthy and over-indulgent dietary habits) and hence may be surprised when diagnosed with gout. Alternatively, they may be embarrassed to admit to the consumption of food and alcohol associated with gout and avoid discussing the diagnosis of gout openly due to concerns about what others may think.

“You don’t brag about it do you?”

Participants may be reluctant to consider that their symptoms are a consequence of gout due to personal beliefs as well.

“I suppose I was a bit in self-denial, I don’t suffer from gout”

Joint aches and pains may also be attributed to other causes including part of the normal ageing process. This may also lead to delayed or missed presentation to a healthcare professional for advice.

“In fact I would put it down to aches and pains getting aged really rather than anything”

“These sort of aches and pains [right] that you think you’re getting as you go into old age, it might actually be linked [mmm] with high uric acid.”

Reduced healthcare utilisation may also result from a lack of trust between the healthcare provider and patient, for example, due to assumptions of high alcohol intake by the former. This may lead to lack of suggested treatment uptake, delayed or missed presentation during recurrence of attacks which result in progressive gout causing poor HRQOL.

“No, you go in, you go in, you're the doctor, how much do you drink? I said I don't drink doctor”

“But as I say it's still treated as a bit of a thing, you know. I think doctors do actually. You know, you've been drinking. How much do you drink?”

Lack of rapport between the patient and healthcare provider may also stem from differences in knowledge, beliefs or attitudes towards the condition. One participant found information from other sources when he did not agree with the physician's views about the cause of his gout.

“I would say my GP almost dismissed my view that [yeah] the attacks were brought on when I stressed the joint, but on the NHS site, definitely it states [yeah] that if you stress a joint it can instigate the gout”

A female participant expressed that her physician was reluctant to refer her to secondary care even when her gout was sub-optimally controlled. This may result from lack of knowledge of when to refer or belief that gout can be managed in primary care by the GP himself. Another participant expressed his dissatisfaction at the physician's attitude or lack of interest towards his condition.

F: “Was your doctor reluctant to send you to erm a gout specialist shall we say?”

“But you couldn't talk to my doctor about it, he wasn't interested”

Gout considered humorous

Denial of the diagnosis of gout or its symptoms may perpetuate lack of awareness of gout in the wider community. Participants felt that their diagnosis of gout and symptoms associated with it were not taken seriously by others.

“I think there's certain diseases that are quite humorous to - and they're not, but they're humorous to everybody else who hasn't got them”

Disbelief in the severity of symptoms by others may also result from their rapid onset.

“It happens so quick, people just don't believe it.”

Dismissal of gout symptoms by others as non-serious may cause unnecessary stoicism and reluctance in reporting recurrent symptoms. Community-wide lack of knowledge about gout and the stigma associated with it as a consequence have also been found previously in a mixed primary and secondary care based study of 11 patients with chronic gout in New Zealand (Lindsay, Gow et al. 2011).

Gout understood only by close contacts

Awareness and understanding of gout was considered better amongst family and friends who realised the severity of symptoms only after being involved in the care or observation of someone who had gout.

“When you’ve got gout your partner or friend or whatever, if they see you with gout when it's bad, they suddenly realise how bad it is”.

Increased awareness of gout by those close to the persons diagnosed with it may lead to earlier presentation for treatment, increased psychological and physical support, which may lead to an improvement in HRQOL.

Lack of information from healthcare professionals

Awareness of gout was lacking not just in the wider community but also amongst healthcare professionals, according to some participants. Participants felt that inadequate information about the causes and treatment of gout was provided by healthcare professionals. This may lead to disbelief in the diagnosis and reduced treatment uptake, both of which could lead to untreated progressive gout with a negative impact on HRQOL.

“We’ve all got ignorance of it. Doctors don't sort of explain exactly what it is”.

Lack of information from healthcare professionals pushed participants to conduct their own search on the internet into the causes and treatments of gout, with some participants expressing concerns over the quality and authenticity of information available via other sources.

"I found out for myself basically. [okay] So the doctor didn't really explain it that well"

The desire for greater healthcare provider-led information was seen amongst participants of my study and those of a US based qualitative in-depth study of patient and providers' views on gout (Harrold, Mazor et al. 2010).

Confusion about dietary causes and restrictions

The area of greatest ambiguity reported by participants was diet and its role in causing and treating gout.

"It's just a great muddle about when it comes to food"

There was a lack of information from 'trusted' sources such as healthcare professionals and participants relied upon both NHS endorsed and unendorsed websites for detailed dietary information. Often self-searched sources of information were considered to have an overwhelming amount of information.

"When I looked onto NHS Direct, after I'd got it, that frightens the life out of you if you do anything because you get five pages".

Confusion over dietary triggers and too many dietary restrictions may lead to poor psychological HRQOL due to lack of enjoyment associated with an extremely restricted dietary lifestyle.

"Oh they put everything on there. What am I going to eat? You have to take it with a pinch of salt".

Participants reported a need for a research program focused on the role of diet in gout through the implementation of individualised food diaries. Such person specific information may help identify a range of dietary triggers.

“Give them a 12 month diary or something like that...and do a research programme like that and maybe you could come up with some facts”

Gout not considered as important as other conditions

Lower priority for research into gout (compared to other conditions considered by participants to arise as a consequence of personal actions such as drug misuse or dependency) was considered synonymous with the lower severity assigned to it compared to cardiovascular diseases or cancers for example. Gout was perceived as less serious as it was considered non-fatal.

“I don't think it's perceived to be life threatening, whereas cancer and heart attacks are “.

This may reflect the lack of awareness of the significant co-morbid conditions associated with it, such as renal impairment, cardiovascular diseases and metabolic syndrome (Roddy, Doherty 2010). Untreated co-morbid conditions in gout may impair HRQOL independent of gout factors (Singh, Strand 2008).

8.2.4 Treatment of gout

Self-management

Participants had tried treating acute attacks of gout with non-pharmacological methods such as ice-packs and cold baths. Modifications in exercise and alcohol intake were also associated with prevention of recurrent attacks.

“When I found out it was gout I changed my lifestyle and stopped drinking”.

Although advocated by the British Society of Rheumatology (BSR) (Jordan, Cameron et al. 2007) and European League Against Rheumatism (EULAR) (Zhang, Doherty et al. 2006a) guidelines as

adjunct treatments, lifestyle modification alone may not reduce serum uric acid below the saturation threshold for formation of crystals that result in recurrent acute attacks, chronic joint pain and formation of tophi (Roddy, Doherty 2010). Therefore on their own, lifestyle modifications may not significantly improve HRQOL which is affected by these gout characteristics (Becker, Schumacher et al. 2009). The understanding of HRQOL linked to urate-lowering treatment and elimination of MSU crystals (therefore curing gout (Hershfield 2009)) was variable amongst the participant group in this study.

Lack of contact with healthcare professional

Obtaining topical or oral non-steroidal anti-inflammatory drugs (NSAID) from the pharmacy was preferred by some participants to presentation to the general practitioner (GP) for treatment. Many confessed to treating recurrent attacks with left over NSAIDs (obtained originally from a previous consultation with the healthcare practitioner).

“Have a supply if I can feel it coming on, because I've got a spare box at home”

The dose of allopurinol was reduced by one participant without medical advice to so. There was some apprehension about the reaction of the healthcare professional when they would find out about the self-directed dose reduction.

“I dropped it down myself to one a day, I don't know what the doctor will say when I tell him”.

Many participants complained of the unavailability of appointments at their GP surgery and the spontaneous resolution of symptoms by the time they were seen.

“So it takes three, like it can take five days to see my doctor. You know, so by the time I get in there it'll probably have eased down a lot”

Lack of presentation to a healthcare professional for treatment of a second or subsequent attacks of gout deters from the opportunity to discuss the association of gout with permanent joint

damage (Chandratre, Roddy et al. 2012) and hence deterioration in HRQOL, which can be prevented through treatment with an urate-lowering agent such as allopurinol. Similarly it may prevent the timely treatment of co-morbid conditions associated with gout which have been independently associated with poor HRQOL (Singh, Strand 2008).

Reluctance to prescribe and take allopurinol

A recurrent participant view was that treatment with allopurinol was not widely advocated by healthcare professionals if the patients had a single or infrequent attacks.

“He says I wouldn't really recommend it if you can get away with it, just come in if you start getting an attack”

Although progressively worse with increasing frequency of attacks, HRQOL was poor even in the presence of one or more attacks in the last 12 months in a number of studies (Khanna, Nuki et al. 2012; Sundy, Schumacher et al. 2006; Lee, Hirsch et al. 2009; Hirsch, Terkeltaub et al. 2010). A second attack is likely to take place within two years of the first attack if gout is left untreated (Roddy, Mallen et al. 2013). However, ULT is recommended for two or more attacks in the last 12 months by the current BSR and American College of Rheumatology (ACR) guidelines (Jordan, Cameron et al. 2007; Khanna, Fitzgerald et al. 2012). Treatment of acute attacks only with NSAIDs were preferred to life-long ULT by many participants and advised by healthcare professionals as seen from the above quotation.

“I find it quite manageable with anti-inflammatory tablets I take for it “

Reluctance to take life-long treatment (allopurinol) was expressed by a few participants despite having no particular concerns regarding allopurinol.

"I find mine just goes quickly, so I'm tremendously happy, I wouldn't want to be on long-term Allopurinol, not because there's anything wrong with it, or anything, or anything else, I'm very, very content with what I've got".

Those who had mild symptoms were content without any treatment at all or quick resolution of symptoms with NSAIDs. It is plausible that they did not consider infrequent or mild attacks of gout to affect their HRQOL.

"He asked me would you like to take a tablet every day of your life and I says not really, no, like you know I really wouldn't want to be on that sort of thing, I said I'd rather stick to it where I can have a tablet and get it"

Although infrequently expressed in the interviews, willingness to take allopurinol was also dependent upon age, with older participants less concerned about taking allopurinol for the remainder of their lives.

"I'm old enough now that another tablet for the rest of my life doesn't make a lot of difference".

Concerns about side-effects of treatment

Lack of information about the possibility of an acute attack due to allopurinol initiation or titration caused concerns about acute attacks in some participants.

"And then you go - and then you get gout, it gives you gout."

Other participants were informed of this possibility but incorrectly advised to discontinue treatment with allopurinol should an acute attack occur.

"My medic said that Allopurinol can actually cause gout to flare up again. If I had any problems, any pain, [yeah] to stop taking it immediately."

Some participants (or their carer) were worried about interaction between allopurinol and other medications taken for co-morbid conditions.

F: *“Because of the other medication that he takes, the gout tablets don’t sit well”.*

“I went back to the doctor again and I said - in the meantime I'd been onto NHS Direct, and the one - Allopurinol is apparently an old pill, an old fashioned one almost, and the new one's that one”

Treatment of gout with allopurinol was considerably harder in the presence of other co-morbid conditions according to some participants

“My kidney function, he always checks because I think it's on the border line, so I think that might have been one of the reasons he was a little bit wary about erm prescribing Allopurinol”.

Similar to my study, variable understanding of the treatment of gout amongst patients has been explored through one-to-one interviews previously (Harrold, Mazor et al. 2010). Lack of information about allopurinol induced attacks as a consequence of urate crystal dissolution and shedding from the joint space (Roddy, Mallen et al. 2013) may cause concerns about continuing treatment and hence adversely affects HRQOL. Pre-empting and monitoring for side effects on the other hand can allow successful urate-lowering treatment which has been shown to improve HRQOL (Khanna, Perez-Ruiz et al. 2011). Fear of drug toxicity and concerns regarding polypharmacy causing adverse drug interactions reported by our participants have also been noted previously (Lipworth, Kerridge et al. 2011; Dalbeth, Petrie et al. 2011).

Perceived benefits of treatment

Those who were aware of what to expect when treatment with allopurinol was started and continued it were content with the results.

“You go two for I think it's two months, I've forgotten now, [yes] and then you go to three, and then that is - that's a miracle”

Treatment with allopurinol was perceived to improve HRQOL. Some participants wished for earlier treatment with allopurinol once they realised that treatment could reduce the frequency of attacks.

“Go to the doctors and get the pills... I wish he'd done it two years ago”

Another reported advantage of treatment with allopurinol was the maintenance of usual dietary lifestyle.

“Well I'm still eating mussels and king prawns and everything like that. The Allopurinol I suppose is to let you do that isn't it?”

8.2.5 The researcher's perspective

As a female person without the symptoms of an inflammatory arthritis such as gout, I have had no experience to draw on during conversations amongst older male participants with gout. However professionally I (the qualitative researcher and interview moderator) have a clinical background currently training as a specialist registrar in Rheumatology. Previous and on-going engagement with patients with gout and review of existing literature on HRQOL in gout may have informed and influenced my personal views prior to data collection for the qualitative study. My own views and experience of diagnosing and treating of gout may influence the interpretation and discussion of the participants' account of how gout and its treatment affect HRQOL. This however is acknowledged as a key feature of the epistemological stance of interpretivism, where the researcher's perspectives and values inevitably influence the findings (Ritchie, Lewis 2003). This also relates to the ontological stance of idealism, which states that reality is an interpretation of the human mind and often influenced by socially constructed meanings (Ritchie, Lewis 2003).

During the interviews, the role of diet and alcohol was central to the experience of participants diagnosed with and treated for gout. As a clinician, even though I am aware of the diet and alcohol as a risk factor for hyperuricaemia, I prioritise pharmacological treatment over lifestyle modification. I was surprised to learn that people with gout may want detailed information about dietary and lifestyle modification, much more than is currently provided. Although the majority were aware of gout as a medical condition, some participants considered it a consequence of a 'natural build-up' of uric acid rather than a 'disease'. They emphasised that gout was different to 'self-inflicted' conditions such as substance misuse or addiction. Such views in my opinion, underpinned their desire to shift blame (placed on them by others for their lifestyle) away from themselves. Even though I am aware of the historical perceptions of gout, I was surprised to learn that it may still be associated with stigma of leading an unhealthy lifestyle, which is essentially what the participants wanted to steer away from by resisting their role in getting gout. The association of gout with co-morbidities is well-recognised in the medical profession but was lacking amongst lay persons with gout. I was surprised that hardly any participants were worried about role of co-morbidities in developing gout and their treatment alongside gout. Although some participants acknowledged that treatment of gout was difficult in the context of co-morbidities such as renal diseases, none attributed co-morbid conditions as a risk factor for hyperuricaemia and gout. Lastly, participants' perception of the impact of gout on HRQOL was limited to acute attacks only. This may stem from the lack of knowledge of the complications of gout in terms of co-morbidity (Mikuls, Farrar et al. 2005a), persistent inflammatory state during inter-critical phases (Soltész, Kerekes et al. 2011) and irreversible joint damage (Roddy, Mallen et al. 2013). As a clinician rheumatologist, these characteristics of gout are well-known to me and play a major role in how gout may affect HRQOL from my perspective.

The potential impact of my expectations from the participants (in the context of my existing clinical knowledge) on the interpretation and analysis of data have been acknowledged where relevant as part of the practice of reflexivity (Ritchie, Lewis 2003) in the discussion section.

8.3 Discussion

The impact of gout and its treatments on HRQOL were represented through three emergent higher order themes- gout characteristics, understanding of gout and treatments for gout. Firstly, gout disease characteristics such as pain and unpredictable nature of attacks were associated with poor physical functioning, fear of making commitments and social isolation. Modifications in lifestyle at home, work and elsewhere were reported by participants as well as by a carer for someone with gout. Secondly a general lack of understanding of gout was evident from perceptions of gout being a disease of over-indulgent lifestyle. Such views may have supported participants in their denial of having gout. Several participants reported a lack of information from healthcare professionals about the causes and treatments of gout, particularly those related to diet. Awareness of gout amongst others (except close family and friends of participants) was also considered to be low. Although not considered fatal or serious in comparison to other conditions by others, participants focused on the excruciating pain associated with it.

Lastly treatment of acute attacks of gout was favoured over urate-lowering treatment with allopurinol by a majority of the participants. Reasons for reluctance to take allopurinol included concerns over side effects and unwillingness to take lifelong medication. Only a small number of participants referred to the reduction in attacks of gout as a benefit of treatment with allopurinol. Other perceived benefits of allopurinol were the ability to continue eating foods such as shellfish.

This study has shown that the symptoms, treatments and understanding of gout affect the physical, psychological and social HRQOL of participants. The impact of gout on physical HRQOL in this study may be evident through its characteristic symptoms of pain and swelling in the affected joint. Reduced mobility due to painful and swollen joint(s) was associated with lack of activity and boredom which could affect the psychological HRQOL. Other factors affecting psychological HRQOL may be the fear of unpredictable nature of attacks and modifications in lifestyle to restrict diet, exercise, work patterns and socialising. A misunderstanding of gout (disease of the rich, overweight, non-serious) may be associated with denial and stoicism which consequently may delay healthcare utilisation. Under treatment of gout may lead to irreversible joint damage and untreated co-morbidities, both of which may be associated with poor overall HRQOL. Participant reluctance to take allopurinol may stem from a lack of understanding of the benefits of treatment and personal concerns about side effects. Both of these issues may be addressed through better information from physicians, a wish expressed almost universally by participants. An improvement in HRQOL was associated with reduced frequency of attacks and being able to maintain usual dietary lifestyle due to treatment with allopurinol.

8.3.1 Adding participants' personal perspective to the results of the quantitative survey

The impact of gout on HRQOL through its symptoms has been common to both the focus group interviews and the questionnaire. The interview data adds a patient focused perspective to the quantitative data in many ways. For example, explaining how the symptoms of an acute attack (such as joint pain and reduced mobility) may have a negative impact on HRQOL by affecting specific activities or emotions (such as running and boredom respectively) may be more meaningful to patients than simply reporting the presence of an acute attack in the questionnaire which may or may not affect their HRQOL depending upon the relevance of the items of the questionnaire to their symptoms. Although the frequency of attacks is clearly an important

determinant of poor HRQOL in the questionnaire, the interview provides an explanation as to what it is about the frequency of attacks (the unpredictable nature of attacks) that has an impact on their psychosocial HRQOL. Routine clinical practice as well as British Society of Rheumatology (Jordan, Cameron et al. 2007), European League Against Rheumatism (Zhang, Doherty et al. 2006a) and American College of Rheumatology (Khanna, Fitzgerald et al. 2012) guidelines focus on the frequency of attacks in determining the initiation of urate-lowering treatment and evaluating treatment success. From the patients' perspective however, the unpredictable nature rather than the frequency of attacks of gout stood out as the main issue that affects HRQOL. The difference in patient and healthcare provider perspective of gout has been reported previously in the context of barriers to effective management of gout (Harrold, Mazor et al. 2010). Treatment with allopurinol was associated with reduced unmet treatment need (compared to those not treated with allopurinol) in the questionnaire but responders had higher concerns about wellbeing during an attack and greater physical disability. In the interviews, those treated with allopurinol were generally in the retirement age group, had recurrent attacks and co-morbid conditions. These factors may lead to lower work productivity and enjoyment of life which form part of the wellbeing during attack sub-scale of the Gout Impact Scale (Hirsch, Terkeltaub et al. 2010). Greater physical disability reported by those on allopurinol in the questionnaire may be explained by the fact that these participants had more severe gout at the outset, an example of confounding by indication. In the interviews for example, participants were more likely to take allopurinol if they had recurrent or unpredictable attacks, which signify severe disease. Thus interview findings add context to the findings of the questionnaire.

Gout was associated with poor HRQOL independent of co-morbidities from the questionnaire-derived data. Similarly, the interview participants were keen to emphasise the importance of gout equal to other co-morbid conditions in having an impact on life. Older age was considered

associated with poor HRQOL in the quantitative survey. It is plausible that older people do not seek medical advice about their symptoms as they consider these to be a part and parcel of normal ageing process, as seen in the interviews. Untreated progressive gout may be associated with the negative impact of gout (Lindsay, Gow et al. 2011). Excruciating pain and swelling of the affected joint(s) reported by the interview participants also represents the features of a 'current attack' which was associated with poor HRQOL in the cross-sectional questionnaire. The interview participants' perception of the impact of gout being dependent upon the location of the joint(s) affected may be similar to poor HRQOL associated with a history of oligo or polyarticular attacks in the questionnaire.

8.3.2 Strengths of the study

To my knowledge this is the first focus group study to evaluate the effects of gout and its treatment on HRQOL. It provides detailed insights into the experiences of living with gout and its treatment in a sub-sample of participants from primary care with chronic gout of varying severity. My study has several strengths in its choice of design and analysis - focus group interaction between participants may have contributed towards uninhibited discussion and emergence of novel themes that may have been difficult to elicit on a one to one basis. Group interactions also promoted exchange of ideas, anecdotes and information, which broaden the experience of participants and add depth to our understanding of the impact of gout. Although initially designed to study the impact of gout and its treatment on HRQOL, the group interactions went beyond these realms and introduced discussions about beliefs and knowledge of gout, both of which link into the impact on HRQOL. The patient sample covered a range of attack frequency over the past one year and just over half of the participants were on ULT (allopurinol), therefore representative of the primary care population with gout in the UK. Participation from a carer for someone with gout added a firsthand perspective of the impact of gout on family and friends.

Independent reviews of the transcripts by three researchers added robustness to the identification of the codes, ensuring they were as close to the participants' views as possible.

8.3.3 Limitations to the study

Limitations of this nested qualitative study include all Caucasian participants which may imply that findings from this study are primarily generalizable to this ethnic group only. However, data from qualitative research is often useful in enhancing understanding of the social phenomenon regardless of its representativeness (Bowling 2009). The initial target sample of 20 participants was unmet due to two unforeseen non-attendances. Although no cut-off point exists to determine an adequate sample size, smaller numbers compared to quantitative studies are appropriate as data collected is often unrestricted in terms of volume, depth and complexity and aims to provide in-depth information about social phenomenon rather than information of statistical relevance (Bowling 2009). The inclusion of two additional participants may not necessarily have added to the codes generated by myself or those provided by the other two reviewers. Hence addition of two more participants may not have delayed theoretical saturation.

Obtaining a true picture of the impact of gout on HRQOL in men and women may be difficult in mixed gender groups, as they may feel socially constrained and unable to contribute freely to discussion (Bowling 2009). This would imply that homogeneous gender group(s) may be more fruitful but in practice a fair representation of women was difficult due to 83.6% participants in the cross-sectional study (source of sampling) being males, as well as the challenging logistics of participant availability, willingness to travel and obtaining a room in the GP surgery. A systematic review (Dirken-Heukensfeldt, Teunissen et al. 2010) has previously shown that females with gout are likely to be older than men, which may pose greater difficulties in getting them to interview venues due to transport and health issues, compared to males with gout.

It is also plausible that some participants may have felt inhibited by the lack of confidentiality in the group setting. However I ensured that all participants engaged equally in the discussions by using verbal and non-verbal prompts. Although largely present in a passive role, the presence of a moderator and research assistant may have influenced the participant responses. Some participants recognized the moderator as a clinician they had met previously, despite efforts on the moderator's part to be present in a non-medical capacity. For all the advantages of an open-ended interview framework, there were some disadvantages such as participants steering the discussion towards the topic of their interest, in this case, diet and its impact on gout symptoms and their lifestyle.

8.3.4 Implications for clinical practice and further research

From the participants' perspective HRQOL is very much influenced by the acute symptoms of gout. However patients need to be made aware of the irreversible joint damage (regardless of joint location and size) associated with untreated chronic gout (Spencer, Carr et al. 2011) which may lead to chronic poor HRQOL over time.

At present there appears to be patient preference for short-term symptomatic treatment of gout compared to ULT. Many participants considered allopurinol to impair their HRQOL through onset of an unexpected acute attack, thereby discontinuing it, occasionally on physicians' advice. Healthcare providers need to be aware and be able to explain to patients that treatment with allopurinol should be continued to see a long-term reduction in serum uric acid (SUA) thereby reducing the frequency of attacks, shrinkage and dissolution of tophi (Perez-Ruiz 2009), leading to an improvement in HRQOL long-term. Patient adherence to treatment may be improved if they understand that through lowering of SUA, allopurinol promotes shedding of SUA crystals from the articular cartilage into the joint space which sets off the inflammatory cascade manifesting itself

as an acute attack, i.e. a sign of successful treatment (Roddy, Mallen et al. 2013). As well as the possibility of onset of an acute attack of gout, they should be advised about its management and the need to continue allopurinol through the duration of the acute attack.

Patients also need to be made aware by healthcare physicians that gout is a recognised independent risk factor for hypertension, renal and cardiovascular diseases (Edwards 2008; Gaffo, Edwards et al. 2009). Early treatment of gout with urate-lowering agent will prevent these complications (Doherty, Jansen et al. 2012). The presence of co-morbidities should be investigated nevertheless and if present, they should be treated alongside gout as they are known to be independently associated with poor HRQOL (Singh, Strand 2008). Greater awareness of gout in the context of co-morbidities (such as hypertension, hyperlipidaemia and diabetes) and genetic susceptibility (Kolz, Johnson et al. 2009) may steer away from the historical perception of gout being self-inflicted and a result of men's excessive intake of alcohol, food and 'debauchery' (Doherty, Jansen et al. 2012). Embarrassment and fear of being ridiculed due to such stereotyping may result in under-reporting of symptoms, therefore lack of treatment. Prompt treatment of symptoms and support from others may be gained through raising community wide awareness of gout. Greater information on the role of diet and exercise from health care providers could also promote lifestyle modification and patient engagement in management of the condition.

Challenges for further research may include gaining in-depth understanding of what makes individuals with gout consult their healthcare provider and the impact this may have on their long-term HRQOL. Their experiences, beliefs and attitudes towards healthcare use for gout could be explored through further qualitative studies. The influence of gender (females) and cultural perceptions or beliefs (different ethnicities) on HRQOL could also be explored through further

qualitative studies. In other studies, females with gout were shown to be more likely than men to have co-morbidities and a more severe form of gout involving multiple number and location of joints (Harrold, Yood et al. 2006; Dirken-Heukensfeldt, Teunissen et al. 2010). Hence females may possibly express poorer HRQOL associated with gout compared to men. Although lack of information from clinicians was a recurrent theme, this was the participants' perception and it may be useful to explore clinicians' perspective on this issue as well as their perceptions of what affects HRQOL in gout.

8.4 Conclusion

The chapters on the quantitative results from the cross-sectional study provided information on *which* factors are associated with poor HRQOL determined by previously designed questionnaires (PF-10, HAQ-DI and GIS). The qualitative study provides a concurrent insight into *why* these, as well as previously unidentified factors, may be associated with poor HRQOL. The qualitative chapter explores in detail what specific characteristics of the questionnaire identified associates of poor HRQOL matter to participants. Participants were given the opportunity to provide detailed descriptive accounts of what affects their HRQOL and prioritise them according to importance. They identified factors such as diet and lack of information, which were not assessed through the questionnaire, as key factors that affect HRQOL in gout. How gout and other characteristics affect HRQOL is participant specific (and not assessed through pre-defined questions). From the key themes identified in this chapter, HRQOL is likely to be affected by characteristics of an acute attack of gout, widespread lack of understanding of what causes gout and lack of information about the role of urate-lowering treatment in preventing progressive disease and its complications. The next and final chapter provides a collective account of the key findings of the various chapters of this thesis and critically evaluates their role in informing the

initial aims and objectives of the thesis as well as their implications for wider primary care clinical practice and research.

9 Thesis conclusions and implications for clinical practice and future research

9.1 Introduction

The idea for this thesis developed from current lack of clinical and theoretical understanding of how Health Related Quality of Life (HRQOL) is affected in people with gout in a routine primary care clinical setting in the UK. Although there are a few existing international studies of HRQOL in gout, they are of limited value in adding to the knowledge base of primary care clinicians and wider public in the UK as they are mostly conducted in specialist settings (secondary care, private clinics, veterans hospital, general health surveys and nested within clinical trials of pharmacological treatments of gout) (Khanna, Nuki et al. 2012; Khanna, Perez-Ruiz et al. 2011; Lee, Hirsch et al. 2009; Singh, Strand 2008 and Dalbeth, Petrie et al. 2011) and may include patients with gout refractory to conventional urate lowering treatment (Becker, Schumacher et al. 2009). Although HRQOL in some of these studies is measured using Outcome Measures in Rheumatology Clinical Trials (OMERACT) validated questionnaires, they are not gout-specific (Khanna, Perez-Ruiz et al. 2011; Lee, Hirsch et al. 2009; Alvarez-Hernandez, Zamudio-Lerma et al. 2009). Only one study to date in primary care in the UK has examined HRQOL in gout but it recruited from two general practices only, measured HRQOL through the WHO-QOL BREF (generic and not validated for use in gout) and had a low participant response (23%) (Roddy, Zhang et al. 2007c).

In light of this, the aim was to establish an in-depth understanding of the burden of gout on HRQOL in the community through a combination of a cross-sectional survey and qualitative focus group interviews by including both generic and gout-specific HRQOL questionnaires and recruiting participants from a large number of general practices. This chapter summarises the key findings

from each of the chapters before discussing the strengths and limitations of the thesis in achieving these findings. The implications of the thesis findings for future research and their role in informing clinical practice are discussed in the final section.

9.2 Summary of key findings of the thesis

HRQOL in gout: A systematic search and overview (chapter 3)

1. *HRQOL in gout is measured using a range of instruments, mostly generic and is poor compared to study controls and normative distributions. Poor HRQOL is associated with gout as well as co-morbid characteristics.*
- HRQOL in gout is measured using a range of generic instruments (11 identified in the systematic review) and a novel gout-specific measure, the GIS. The SF-36 and HAQ-DI had overall more robust clinimetric properties compared to the GIS and have previously been validated by the OMERACT group for measurement of HRQOL in studies of chronic gout (Singh, Taylor et al. 2011; Schumacher, Taylor et al. 2009).
- All but one study were based outside the UK and limited by their specialist settings, inclusion of complex cases of gout or those refractory to standard urate-lowering treatments (ULT), exclusive use of either generic or gout-specific measures.
- Gout characteristics implicated in poor HRQOL are as follows: frequency of attacks, pain during attack and pain in between attacks, number of joints involved in an attack, time between attacks and patient rated severity. Evidence for association of HRQOL with tophi, SUA and treatment with allopurinol was variable.
- Medical co-morbid conditions in gout contribute to poor HRQOL and increased healthcare resource utilisation

Cross-sectional survey of HRQOL in gout: Response and responder characteristics (chapter 5)

2. Responders to the cross-sectional survey were likely to be older, male and live in the least deprived neighbourhood compared to non-responders

- An adjusted response of 65.9% was seen in this study
- 36.7% of the participants had a history of oligo or polyarticular attacks and 43.9% had between one and three attacks over the last 12 months.
- 56.3 % were on allopurinol and the median dose was 300 mg per day.
- The mean SUA was 441 $\mu\text{mol/L}$ and tophi were documented for 2.3% of the participants who consented for medical record review.
- The commonest self-reported co-morbidities were hypertension, body pain, hyperlipidaemia, diabetes and angina.
- At least 10% of the participants reported mild anxiety and depression in the GAD-7 and PHQ-9 respectively.

The association of gout, co-morbid and socio-demographic characteristics with HRQOL:

Univariate analysis (chapter 6)

3. Mild to moderately impaired HRQOL was seen in the presence of gout, co-morbid and socio-demographic characteristics.

- Mean HRQOL was lower in those with (compared to without) a current attack, a history of oligo or polyarticular attacks and increasing frequency of attacks over the last 12 months.
- SUA below treatment target ($< 360 \mu\text{mol/L}$) and treatment with allopurinol (compared to not being on allopurinol) were associated with lower unmet treatment need in the GIS.
- However those on allopurinol $> 300 \text{ mg per day}$ reported worse HRQOL than those who were on $< 300 \text{ mg per day}$.

- Mean HRQOL was also lower in those with (compared to without) ischaemic heart disease, stroke, anxiety, depression, body pain and renal failure.
- Mean HRQOL was lower in the presence (compared to the absence) of the following socio-demographic characteristics: non-Caucasian ethnicity, most deprived neighbourhood, female gender, extremes of Body Mass Index (BMI) and lack of further education.

The cross-sectional association of gout, co-morbid and socio-demographic characteristics with HRQOL: A linear regression analysis (chapter 7)

4. *Gout was independently associated with HRQOL even after adjustments for co-morbid and socio-demographic characteristics in multivariate linear regression models.*
- Poor HRQOL was associated with frequency of attacks over the preceding 12 months, currently having an attack of gout (GIS only), a history of oligo or polyarticular attacks, SUA (GIS only) and treatment with allopurinol.
 - HRQOL measured by GIS was associated exclusively with psychological co-morbidities (anxiety and depression) and body pain but psychological as well as physical co-morbidities were associated with poor HRQOL in the generic questionnaires.
 - Older age (compared to younger age) and female gender (compared to male) were associated with poor HRQOL independent of all other socio-demographic and disease characteristics.

The impact of gout and its treatments on HRQOL: A qualitative study of participants' perspective using focus group interviews (chapter 8)

5. *HRQOL in gout is associated not just with disease-specific characteristics but also with misunderstanding due to lack of information and persistence of historical negative views about gout in the community.*

- Gout characteristics such as pain, unpredictable nature of attacks, location of joint involved in an attack and functional limitation causing changes in lifestyle were considered to have negative impact on HRQOL
- Misunderstanding of gout (wider and stereotypical association with unhealthy lifestyle), lack of information from healthcare professionals about causes and treatments of gout adversely affected HRQOL.

9.3 Discussion of key findings of the thesis

Despite being the commonest inflammatory arthritis with a prevalence of 2.49% (Kuo, Grainge et al. 2014) in the UK, HRQOL in the context of gout remains under-researched in the UK. Current understanding of HRQOL in gout has been informed by studies largely based outside the UK using populations that may not be representative of those with gout seen in a typical UK general practice. Majority of these studies have used generic HRQOL measures which measure health and functional limitations broadly and allow comparison across different disease states but may not be specific to the impact of gout per se. The newly developed GIS is specifically designed to assess the impact of gout on all domains of HRQOL but to date remains unendorsed by OMERACT due to unfamiliarity of the concepts it tries to measure and concerns over the measurement properties of some of its sub-scales (Singh, Taylor et al. 2011). Given the above, the generalisability of the findings of existing studies to the local population and their implications towards local clinical practice is debatable.

To overcome some of the above issues highlighted by the systematic review, a UK primary care-based cross-sectional survey of HRQOL measured using a combination of generic and gout-specific questionnaires was conducted. The results of this study show that the gout characteristics and their impact on HRQOL vary greatly amongst patients managed in primary care. Patients in primary care may have a range of presentations of gout, which may be less severe when compared to those managed in specialist settings. Never the less gout remains under-treated with just over a half of the participants taking ULT in the form of allopurinol. The mean SUA (441 $\mu\text{mol/L}$) remains above the recommended target threshold for treatment and dissolution of tophi (Doherty, Jansen et al. 2012). This study also highlighted the highly prevalent co-morbidities associated with gout which may contribute to its overall impact on HRQOL.

This multi-factorial impact of gout was illustrated by lower mean HRQOL scores in the presence of participant reported (current attack, frequency of attacks, history of oligo/polyarticular attacks, treatment with allopurinol, co-morbidities) and objective (SUA > 360 $\mu\text{mol/L}$, older age, female gender, neighbourhood deprivation) characteristics. It is biologically plausible that disease severity (manifested by increasing frequency of attacks, history of oligo/polyarticular attacks, hyperuricaemia) is associated with poor HRQOL in gout. However the association of treatment with allopurinol and older females with poor HRQOL may be confounded by indication (more severe disease in these two groups compared to those untreated or younger males).

The underpinning hypothesis for this thesis was that gout was associated with poor HRQOL independent of co-morbid or socio-demographic characteristics. Therefore the independent association of gout with HRQOL was examined through multivariate linear regression analyses. Even after adjusting for other gout, co-morbid and socio-demographic characteristics, frequency of attacks, current attack, history of oligo/polyarticular attacks, SUA and treatment with

allopurinol remained associated with poor HRQOL. The association of current attack and SUA with HRQOL were seen exclusively in the GIS. The association of allopurinol with HRQOL has not been seen previously in the only existing UK primary care-based study (Roddy, Zhang et al. 2007c). The link between gout characteristics (unpredictable nature of attacks, pain intensity, pattern of joint affected in attacks) poor physical (changes in lifestyle due to functional limitations) and psychological (isolation, boredom, crying) HRQOL were seen in the qualitative study. Urate-lowering treatment can lead to dissolution of monosodium urate (MSU) crystals and prevent further crystal formation (Zhang, Doherty et al. 2006a), thereby curing gout and as such should be initiated early to prevent gout affecting HRQOL. By definition HRQOL is:

“The value assigned to the duration of life as modified by impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy”

(Patrick and Erikson. 1993, p.419)

Hence the value or quality of life may also be influenced by the impact of conditions other than gout (co-morbidities) and social context. For this reason, the role of these two domains in HRQOL in gout was also examined in the cross-sectional survey. In addition to the traditionally associated co-morbid conditions (diabetes, renal failure, hypertension, cardiovascular disease), HRQOL was adversely affected by anxiety, depression and body pain, independent of gout and socio-demographic characteristics. Although treatment of physical co-morbidities alongside gout is advocated by current guidelines (Jordan, Cameron et al. 2007; Zhang, Doherty et al. 2006a; Khanna, Fitzgerald et al. 2012), anxiety and depression remain relatively neglected.

Therefore there is a case for on-going education about the management of both physical co-morbidities and anxiety/depression in the context of gout. The association of female gender and older age with HRQOL independent of gout and co-morbid characteristics should alert clinicians to

target early treatment in these two groups before HRQOL is impaired or worsens further. The qualitative study provides evidence that older participants may not consult for gout due to mistakenly assuming joint symptoms as part of the normal ageing process. There was a general lack of awareness amongst participants that women can get gout, which may lead to low rates of healthcare utilisation in this group as well.

9.4 Strengths and limitations of the thesis

The strengths and limitations specific to each objective of the thesis have been discussed previously within their corresponding chapters. This section presents a broader reflection on the strengths and limitations of the thesis as a whole.

9.4.1 Strengths

First, the thesis presents a comprehensive systematic review of the existing literature on HRQOL in gout and the instruments used to measure this. The findings of this review informed the larger cohort study design within which this cross-sectional study is nested.

Second, this thesis presents original research in the form of a cross-sectional study of HRQOL in gout in primary care. Since the endorsement of HRQOL as an important outcome measure in studies of chronic gout by OMERACT 8 in 2006 (Schumacher, Taylor et al. 2007), research in this domain is ever expanding. However there has been limited examination of HRQOL in UK primary care and none using both generic and the newly developed GIS to measure HRQOL. This thesis is a novel examination of HRQOL measured by generic questionnaires (PF-10, HAQ-DI) and GIS to in a non-selective UK primary care population. This thesis is therefore an important addition to the field of HRQOL in gout research.

This is the first large-scale cross-sectional study of HRQOL in gout in UK with 1184 (65.9%) responses. The study used techniques previously shown to boost response, such as personalised invitations, reminder letters and clear and large font in all study documents (Edwards, Roberts et al. 2002). As 98% of the population are registered within the UK general practice (Bowling 2009), recruitment from general practice is likely to include the vast majority of people with gout, which is where gout is predominantly managed (Dalbeth 2013). By having a narrow exclusion criteria (see chapter 4: Study design and methods for details) participants with a range of gout characteristics would have been included in the study. Recruitment from primary care also ensures that the study sample is representative of the majority of people with gout who are treated in primary care. A comprehensive range of gout, co-morbid and socio-demographic characteristics are included in the questionnaire. This is the first UK based study to examine HRQOL in gout using a combination of validated generic and newly developed gout-specific measures of HRQOL and clinically validated tools to assess anxiety (GAD-7) and depression (PHQ-9). Linking self-reported questionnaire data to medical record allowed assessment of the association of HRQOL with objective measures which participants may not be aware of or able to recall, such as SUA and tophi. The ethical conduct of the research in this thesis is approved by the local Research Ethics Committee (REC reference number: 12/NW/0297, see appendix 16).

Third, the demographic composition of the study responders (mostly male, middle or older age-group and Caucasian) reflects their representativeness of a typical population with gout in the geographical area (West Midlands) within which the study is set⁴³. The inclusion of socio-demographic data (for all identified participants) from general practice record allowed comparison between responders and non-responders. The frequency of missing data was limited to $\leq 10\%$ for all gout, co-morbid, socio-demographic and HRQOL variables (except a few items in

⁴³ <http://www.nomisweb.co.uk/census/2011/KS201EW/view/2013265925?cols=measures>

the GIS well-being during attack and HAQ-DI) and sample multiple imputation did not improve the β coefficient or its 95% CI significantly enough in the linear regression analysis. Hence it was not deemed necessary (after discussion with study statistician Dr M Bucknall) to impute for missing data in this study.

Fourth, the association of HRQOL with gout, co-morbid and socio-demographic characteristics were examined initially through comparison between mean HRQOL scores stratified by the explanatory variables. This allowed ascertainment of the distribution of poor HRQOL in gout. However to examine the independent association of gout (as well as co-morbid and socio-demographic characteristics) with HRQOL, unadjusted and adjusted multivariate linear regression analysis was performed. Techniques to minimise the impact of missing data on the adjusted multivariate analysis were to include only those who consented to medical record review when examining tophi and SUA. For SUA specifically, only those who had a level recorded were included in the linear regression analysis. Similarly for the dose of allopurinol, only those who reported taking allopurinol were included in the analysis. The multivariate model provided estimates of association (β coefficient, 95% CI) for each variable adjusted for all other variables in the model. Therefore the effect of all measured potential confounding variables was accounted for.

Finally, the inclusion of the qualitative study adds to the in-depth understanding of how gout and its treatments affect HRQOL from the patients' perspective. It provides detailed insight into how and why some of the variables identified from the questionnaire affect HRQOL. It also adds new dimensions to the understanding of HRQOL in life through identification of concepts not explored through the questionnaire (misunderstanding of gout and lack of information). The results of the qualitative study not only highlight disease characteristics that need to be addressed by the

clinicians but also patient agendas pertaining to diet, lifestyle modification and the psychological impact of gout.

9.4.2 Limitations

The principal criterion for inclusion into this study was a diagnosis of gout based on Read Code classification within participating general practices which undergo regular training, assessment and feedback to ensure the quality of the computerised morbidity coding (Porcheret, Hughes et al. 2004). The method of diagnosis of gout however was not determined in this study and is likely to have been on clinical grounds as the gold standard method of identification of MSU crystals from synovial aspirate is infrequently performed in primary care (Roddy, Zhang et al. 2007c). Although there is a possibility of misclassification of atypical presentations (Wolfe, Cathey 1991) previous studies of gout have also considered primary care diagnosis (Annemans, Spaepen et al. 2008; Mikuls, Farrar et al. 2005a; Pal, Foxall et al. 2000; Mikuls, Farrar et al. 2005b). To add validity to the primary care diagnosis of gout, a previous study of gout nested in the primary care consultation database (CiPCA) has shown that free text consultations were generally consistent with the diagnosis of gout (Roddy, Mallen et al. 2010) and a primary care diagnosis of gout was concordant with diagnosis by a rheumatologist in 83% of the cases (Roddy, Zhang et al. 2007a).

Although self-reported data in this study may be subject to inaccuracy due to recall bias or participant reporting to suit researcher preference, using medical records alone may result in under-estimation of symptoms based conditions (Skinner, Miller et al. 2005) particularly if patients do not always consult their clinician as acknowledged in gout (Spencer, Carr et al. 2012). In addition, the concordance of self-reported data with medical record has been validated previously in studies of self-reported urate-lowering treatment and colchicine uptake compared to electronic medication event monitoring (de Klerk, van der Heijde et al. 2003), comparison of pharmacy claims data and self-reported use of antidepressants (Kwon, Bungay et al. 2003) and

concordance between ambulatory medical records and patient survey data in the context of chronic diseases (diabetes, ischaemic heart disease, chronic obstructive pulmonary disease and low back pain) (Tisnado, Adams et al. 2006). The reliability and sensitivity of self-reported physician diagnosis of gout in epidemiological studies was further validated in the Campaign Against Cancer and Heart Disease (CLUE II) and Arthrosclerosis Risk in the Community (ARIC) cohorts (McAdams, Maynard et al. 2011). In the CLUE II cohort, of the 247 participants reporting gout at baseline, 65% reported gout at the three follow-up time-points. The age of onset of gout was also accurately reported by the 190 participants in 2003 and 2007 (Spearman correlation coefficient 0.85 and participants reporting older age at onset in 2007 compared to 2003). In the ARIC cohort, the sensitivity of self-reported physician diagnosis of gout compared to diagnosis of gout at hospital discharge or prescription of a gout medication was 84% (McAdams, Maynard et al. 2011).

The low frequency of female and non-Caucasian participants in this study may be a limitation to understanding the effect of gout on HRQOL in these sub-groups. In the future, purposive quota sampling (Upton, Cook 2008) may be useful in improving the participation of these groups. A greater than previously seen frequency of participants reported treatment with allopurinol in this study (56.3%). Participants on allopurinol may have more severe disease than those untreated with allopurinol or concerns about side-effects hence they may be more inclined to participate in the study (response bias). Although presence of any body pain in the preceding 4 weeks was ascertained, the location of pain was not determined from the manikin to be able to differentiate gout and non-gout associated pain. Patients with other causes of inflammatory joint symptoms (rheumatoid arthritis, seronegative spondyloarthritis, inflammatory osteoarthritis) that may present similarly to gout were not excluded hence it is possible that some participants may have attributed their symptoms to gout when in fact it may be due to another rheumatological

condition. A significant association between sites of acute attacks of gout and osteoarthritis (OR 7.94; 95% CI 6.27, 10.05) has been reported previously (Roddy, Zhang et al. 2007a). Excluding participants based upon the co-existence of one or more of these rheumatological diseases however may have significantly reduced the number of eligible participants.

Although a comprehensive range of potential confounding co-morbid and socio-demographic confounding factors were measured in the cross-sectional questionnaire, other unmeasured confounders (pharmacological treatments other than allopurinol and colchicine such as NSAIDs or steroids) remain unaccounted for in the associations between HRQOL and explanatory variables presented in this thesis. Tophi and SUA ascertainment was within the two years preceding the study and hence may not necessarily be representative of HRQOL at the time of questionnaire completion for some participants.

Finally, due to the structure of doctoral training, the data collection for the qualitative study was concurrent with the cross-sectional questionnaire survey. Therefore the interview questions were not specifically designed to further explore issues identified in the epidemiological analysis. Nevertheless the two methodology approaches were complementary to each other, as discussed in chapter 8 (The impact of gout and its treatments on HRQOL: A qualitative study of patients' perspectives using focus group interviews).

9.5 Implications for future research

This thesis has shown that HRQOL is poor in those with markers of severity of gout (increasing frequency of attacks, history of oligo or polyarticular attacks, SUA above treatment target and treatment with allopurinol). Evidence for association of HRQOL with objective clinical

characteristics however was weak – SUA > 360 µmol/L was only associated with unmet treatment need in the GIS and no association was seen with tophi. Hence this thesis presents an argument for further studies to investigate the role of tophi and SUA in HRQOL in gout. To strengthen the evidence base for the association of HRQOL with clinician derived disease characteristics, future studies could include physician-rated severity and radiographic changes of gout. The site-specific impact of gout on HRQOL could also be explored as participants in the qualitative interview suggested severity of gout was dependent upon the joint(s) affected. Anxiety and depression were associated with HRQOL in gout in the PF-10, HAQ-DI and GIS. However their role in gout remains under-researched as only one study (Singh, Strand 2008) in the systematic review identified depression as a key associate of HRQOL. Despite this, it is clear that there is a link between gout and psychological health, as evidenced by the lower scores for mental health (Picavet, Hoeymans 2004) and mental component summary scores in the SF-36 (Khanna, Ahmed et al. 2008; Singh, Strand 2008; Lee, Hirsch et al. 2009) in those with gout compared to those without gout or normative distributions. Previous qualitative studies have also shown that people with gout often have poor psychological health through feelings of isolation, pain, poor sleep and dependency on others (Lindsay, Gow et al. 2011; Singh 2014). The use of generic questionnaires and specialist settings of these studies however suggest that further research should evaluate the role of anxiety and depression in HRQOL in gout in primary care using the gout-specific GIS in addition to generic questionnaires.

Gout is a relapsing remitting condition and it is plausible that HRQOL fluctuates between acute and inter-critical gout. It is increasing evident however that a chronic inflammatory state persists even in inter-critical periods leading to chronic synovitis leading to cartilage loss and bone erosion (Choi, Mount et al. 2005). Whether this affects HRQOL to the same extent as features of acute

attack could be explored by performing sub-group analysis on those with self-reported acute attack versus those who do not report an attack at the time of the study.

Treatment with allopurinol and higher doses were associated with poor HRQOL. Disease characteristics of those treated with and without allopurinol could be compared to support the theory of confounding by indication. Additionally though linkage to medical (prescription) records, the effect of co-prescription of other urate-lowering or anti-inflammatory treatments on HRQOL could be explored. The use of NSAIDs and other non-pharmacological treatments were commonly reported by participants in the qualitative study and are likely to have an association with HRQOL. Linkage of survey to medical records could also provide an estimate of the concordance between self-reported and medical record derived data.

Another area of participant interest in the qualitative study was the role of diet in the treatment of gout. The association of dietary modifications with HRQOL may be of great interest to patients and provide further evidence for the integration of lifestyle modification into standard treatment advice provided by clinicians. Food and activity diaries could therefore be included as part of patient-reported data in future studies.

Although useful in presenting a comprehensive evaluation of gout-specific associates, there was a discrepancy between HRQOL measured in two sub-scales of the GIS. Although allopurinol was associated with lower unmet treatment need, it was associated with higher concern over well being during attack. Further studies could explore the internal consistency and construct validity of the unmet treatment need subscale, which are areas of concern identified by the OMERACT 10 group (Singh, Taylor et al. 2011). Another approach to providing explanation for this and other

findings from the questionnaire would be to do a sequential analysis with the quantitative results informing the interview guide used in the qualitative study.

The prospective nature of the cohort study within which this cross-sectional study is nested allow future research studies to examine which of these associates predict longer-term HRQOL and identify novel disease characteristics that may not necessarily be associated with HRQOL at baseline. This approach may help the early identification of individuals who are at risk of developing more severe gout and hence worse HRQOL who should be targeted for early urate-lowering treatment. Finally as acknowledged previously, the findings of this study may be of limited generalizability to females and ethnically diverse populations. Hence future studies may wish to focus on the under-researched HRQOL in these population sub-groups.

Associations of gout, co-morbid and socio-demographic with HRQOL vary according to the questionnaire used. For example, HRQOL measured using the GIS only was associated with SUA and currently having an attack of gout and HRQOL measured using the generic questionnaires only was associated with medical co-morbidities and gender. Therefore the choice of questionnaires in future research studies should be based upon the objectives of the study.

9.6 Implications for clinical practice

The findings of this thesis can inform clinicians in primary care to be aware that gout features and co-existing co-morbidities are associated with poor HRQOL in gout. Patients with gout characteristics such as one or more attack in the preceding 12 months, history of oligo or polyarticular attacks, acute attack, SUA > 360 $\mu\text{mol/L}$ and co-morbidities need to be identified and treated early to prevent disease progression and poor HRQOL. If started early enough, urate-

lowering treatment may prevent the development of above characteristics and poor HRQOL. Current guidelines recommend starting ULT at ≥ 2 attacks per year (Jordan, Cameron et al. 2007; Khanna, Fitzgerald et al. 2012) or according to clinical judgement (Zhang, Doherty et al. 2006a) but do not include other associates of poor HRQOL identified in this study. Co-morbid conditions (well-recognised as well as under-associated with gout such as anxiety and depression) should be treated alongside gout. Although current guidelines recommend treatment of associated physical co-morbidities (Jordan, Cameron et al. 2007; Khanna, Fitzgerald et al. 2012; Zhang, Doherty et al. 2006a), they do not identify psychological co-morbidities as areas that need addressing. Despite the existence of the BSR (Jordan, Cameron et al. 2007), EULAR (Zhang, Doherty et al. 2006a) and ACR (Khanna, Fitzgerald et al. 2012) guidelines for the management of gout, HRQOL in gout remains impaired due to under-treatment, misunderstanding and lack of information about gout. Therefore there is a need for on-going education of trainees, general practitioners, specialists as well as the lay public.

Females and older people with gout are susceptible to poor HRQOL and should be treated as those at risk of poor outcomes by clinicians with careful monitoring and appropriate early treatment. Poor HRQOL encompasses multiple domains of life including work productivity, activity impairment and healthcare utilisation (Khanna, Nuki et al. 2012). Greater healthcare utilisation in people with gout has implications for costs associated with medical and prescription claims, short-term disability, workers compensation and work absence (Wu, Forsythe et al. 2012). A study of gout refractory to conventional ULT reported an average annual workday loss of 25 days (Brook, Kleinman et al. 2006). Preventing poor HRQOL may significantly alleviate the burden on primary care resources.

9.7 Conclusion

HRQOL has received increasing attention in the last decade due to increasing understanding of gout pathogenesis, treatment and the paradigm shift from the previous emphasis on end-organ failure or mortality to patient-reported outcomes. Research into HRQOL in gout nevertheless has been limited in primary care in the UK. Most international studies are based within specialist settings and use generic measures of HRQOL.

The findings described in this thesis provide evidence to support the underlying hypothesis that HRQOL is poor in gout independent of co-morbid and socio-demographic characteristics and remains poorly recognised and managed in primary care. A more comprehensive assessment of HRQOL may be achieved through a combination of generic and gout-specific questionnaires. Patient-reported gout characteristics as well as SUA > 360 $\mu\text{mol/L}$ are associated with poor HRQOL. Co-morbid conditions (including anxiety and depression) and socio-demographic characteristics (older age and female gender) are also contributory towards poor HRQOL in gout. From the patients' perspective unpredictable nature of attacks, gout characteristics acting as a barrier to usual lifestyle, diet and misunderstanding of gout have an important role in HRQOL. Patient priorities however may not necessarily be concordant with those of clinicians. Patient need for more information on all aspects of gout including non-pharmacological management remains unmet as yet.

Despite the long-standing awareness that gout remains poorly managed in primary care in the UK, poor HRQOL identified in this thesis is reflective of a lack of progress in this area. By recognising the factors identified as associates of poor HRQOL in this thesis, those at risk of poor outcome may be offered early and holistic interventions to prevent disease progression.

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Appendix 1: Health-related quality of life in gout: a systematic review

Original article

Health-related quality of life in gout: a systematic review

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Abstract

Objectives. To identify the instruments that have been used to measure health-related quality of life (HRQOL) in gout and assess their clinimetric properties, determine the distribution of HRQOL in gout and identify factors associated with poor HRQOL.

Methods. Medline, CINAHL, EMBASE and PsycINFO were searched from inception to October 2012. Search terms pertained to gout, health or functional status, clinimetric properties and HRQOL. Study data extraction and quality assessment were performed by two independent reviewers.

Results. From 474 identified studies, 22 met the inclusion criteria. Health Assessment Questionnaire Disability Index (HAQ-DI) and Short Form 36 (SF-36) were most frequently used and highest rated due to robust construct and concurrent validity, despite high floor and ceiling effects. The Gout Impact Scale had good content validity. Gout had a greater impact on physical HRQOL compared to other domains. Both gout-specific features (attack frequency and intensity, intercritical pain and number of joints involved) and comorbid disease were associated with poor HRQOL. Evidence for objective features such as tophi and serum uric acid was less robust. Limitations of existing studies include cross-sectional design, recruitment from specialist clinic settings and frequent use of generic instruments.

Conclusion. Most studies have used the generic HAQ-DI and SF-36. Gout-specific characteristics and comorbidities contribute to poor HRQOL. There is a need for a cohort study in primary care (where most patients with gout are treated) to determine which factors predict changes in HRQOL over time. This will enable those at risk of deterioration to be identified and better targeted for treatment.

Key words: gout, health-related quality of life, clinimetrics.

Introduction

Gout is the most prevalent inflammatory arthritis, affecting 1.4% of adults in Europe [1]. Health-related quality of life (HRQOL) may be adversely influenced by the excruciating pain, chronic arthropathy, associated co-morbidities (renal and cardiovascular disease, metabolic syndrome and OA) and frequent suboptimal management in gout [2]. The UK Department of Health and the Outcome Measures in Rheumatology Clinical Trials (OMERACT) group have identified HRQOL as a key component of

patient outcome assessment alongside the more traditional markers such as survival rates, symptoms and cost of resources [3, 4]. HRQOL can be measured using generic instruments, which allow HRQOL to be compared between different disease states, or by disease-specific instruments, which account for the specific facets of individual diseases [5]. Recent interest in HRQOL in gout patients has resulted in the development of a disease-specific measure, the Gout Assessment Questionnaire 1.0 [6], which was subsequently revised, resulting in the Gout Assessment Questionnaire 2.0 and its subscale, the Gout Impact Scale (GIS) [7]. The aims of this systematic review were to (i) describe which instruments have been used to measure HRQOL in gout in existing studies, (ii) describe the clinimetric properties of these instruments, (iii) describe the distribution of HRQOL in gout and (iv) identify which factors associate with poor HRQOL in gout.

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Methods

Search strategy

A systematic search was undertaken using the following databases from inception to October 2012: Medline, EMBASE, CINAHL, PsycINFO and Cochrane database of systematic reviews. The search aimed to identify studies of self-reported HRQOL in gout as well as those evaluating the clinimetric (measurement) properties of instruments used to assess HRQOL in gout patients. Clinimetrics is defined as a methodological discipline focused on measurement issues [8, 9]. The clinimetric properties of an instrument describe the quality of its clinical measurements, e.g. validity, reliability and responsiveness. Search terms included gout, health or functional status and HRQOL. These domains were combined with filters for measurement properties, such as elicitation method (scale, measure and questionnaire) and measure of scientific quality (psychometrics, validity, responsiveness, reliability) [10].

To increase the recall of the search results, all terms were typed as synonyms and free text and mapped to a thesaurus. Truncated terms and wildcards were used specific to each database.

Eligibility criteria

The following inclusion criteria were applied: (i) adults aged >18 years with gout, (ii) assessment of HRQOL or evaluation of the clinimetric properties of one or more instruments and (iii) publication in English. Both primary care and secondary care studies were included. Publications without empirical data (such as commentaries, editorials and reviews), randomized controlled trials deemed to be non-representative of a typical population with gout and articles not available as full text were excluded.

Study selection

Titles and abstracts of identified articles were independently reviewed against the criteria above by two reviewers (PC, LC). Articles that could not be excluded based on title and abstract screening alone were included for full-text review, carried out independently by the same two reviewers. Further exclusions were made based on re-application of the inclusion and exclusion criteria. The references of all full-text papers were examined for relevant studies. Disagreements at all stages were arbitrated through consensus meetings.

Data extraction

The following data were extracted: study design (length and method of recruitment, inclusion and exclusion criteria, controls), participants (sample size, geographic location, setting, mean age, gender, ethnicity, method of gout diagnosis), study response rate or attrition, methods of measurement (follow-up, statistical analysis), HRQOL scores and factors associated with poor HRQOL. The Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) checklist was used

to extract data on the clinimetric properties of questionnaires [11].

Methodological assessment

The quality of the following clinimetric properties of HRQOL instruments was assessed against a modified version of the quality criteria for measurement properties by Terwee *et al.* [12]—validity (content, known group, floor or ceiling effects, construct and concurrent), reliability (internal consistency and test-retest) and responsiveness. Qualitative studies were assessed against the criteria set by the Critical Appraisal Skills Programme (CASP) [13]. Cohort studies were assessed against the standards set by the Newcastle Ottawa Scale (NOS) for assessing the quality of non-randomized studies [14]. Assessment of the methodological quality of cross-sectional studies included modified components such as the baseline associates of HRQOL, response rate and a measure of association between poor HRQOL in gout compared with controls, in addition to the NOS quality assessment scale.

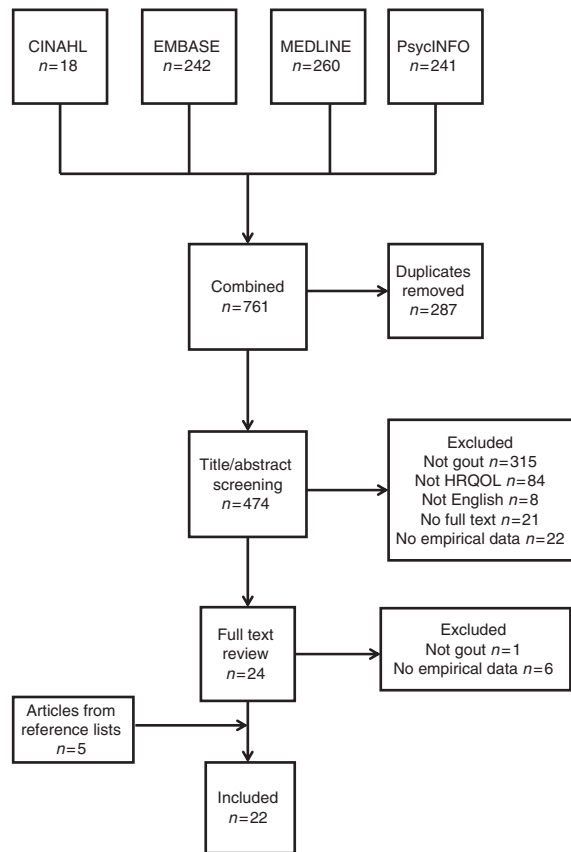
Results

Study selection

A total of 761 potentially relevant articles were identified: 474 articles were included in title and abstract screening after removal of duplicated papers. After full-text review of the remaining 24 articles as well as 5 articles identified from reference lists, 22 articles met the inclusion criteria. Reasons for exclusion are described in Fig. 1. Included studies are summarized in Table 1.

Study characteristics and methodological quality

Of the 22 included studies, 8 evaluated clinimetric properties of instruments used to measure HRQOL [4, 6, 7, 15–19] and the remainder focused on self-reported HRQOL or health care utilization [20, 21–32]. One study reported both the measurement properties as well as the scores of HRQOL as measured by the Health Assessment Questionnaire Disability Index (HAQ-DI) and Short Form 36 (SF-36) [33]. All studies were published in or after 2006. A total of 13 cross-sectional [4, 7, 18, 20–24, 26–30], 7 cohort [6, 15–17, 19, 25, 33] and 2 qualitative studies [31, 32] were identified. The median sample size of the 20 quantitative studies was 134 (range 49–70 334). Only four studies [17, 18, 22, 33] used the diagnostic gold standard of MSU crystal identification from joint or tophus aspirate [34]. Other methods of gout diagnosis in studies included hyperuricaemia ($n=3$) [6, 18, 19], ACR classification criteria [35] ($n=11$) [4, 7, 15, 16, 23, 25, 26, 28, 29, 31, 35], self-reported gout ($n=4$) [19, 21, 22, 30], physician diagnosis ($n=2$) [22, 24] and ICD-9 codes ($n=1$) [20]. The follow-up period in cohort studies ranged from 8 weeks [16, 19] to 2 years [17]. Five cross-sectional studies reported response rates of >60% [7, 18, 22, 24, 29]. Quality assessment of cohort and cross-sectional studies is summarized in Table 2 (for qualitative studies, see supplementary Table S1 available as supplementary data at *Rheumatology* Online).

Fig. 1 Systematic search and study selection.

Instruments used to measure HRQOL in gout

Twelve different instruments to measure HRQOL were identified (five studies employed more than one instrument) [16, 18, 23, 25, 33]. Most commonly used were the HAQ-DI ($n=6$) [4, 15, 18, 23, 27, 33], SF-36 ($n=5$) [17, 20, 22, 23, 33], GIS ($n=4$) [7, 19, 24, 26] and Health Assessment Questionnaire II (HAQ II, $n=2$) [18, 25]. The Gout Assessment Questionnaire 1.0 (GAQ 1.0) [6], Arthritis Impact Measurement Scale (AIMS) [16], Medical Outcomes Survey 20 (MOS 20) [16], Brief Illness Perception Questionnaire (BIPQ) [25], SF-36 Physical Function 10 (PF10) [18], Short Form 12 (SF-12v2) [30], HAQ [28], EuroQOL 5D (EQ5D) [23], Short Form 6D (SF-6D) [30] and World Health Organisation Quality of Life (WHOQOL)-BREF [21] were each used once.

Clinimetric properties of instruments used to measure HRQOL in gout

Values of the measurement properties of identified instruments are available in Table 3. Supplementary Tables S2 and S3 (available at *Rheumatology* Online) present quality ratings assigned to the measurement properties assessed against the modified guidelines by Terwee *et al.* [12]. Content validity was only established for the gout-specific GIS and GAQ 1.0, which received patient and health care

provider input during the development of the questionnaires [6, 7]. The generic SF-36 (except PF10 [18]) and the HAQ-DI [4, 15–17, 33] performed well in the known-group analysis based on self-reported general health, comorbidities and correlation with disease characteristics. The HAQ-DI, HAQ II and SF-36 had significant floor (HAQ-DI 20.5%) and ceiling (HAQ-DI 34%, HAQ II 25.8%, SF-36 18.4%) effects, indicating a weakness in the ability to differentiate between participants at the extreme ends of the scale (no disability and severe disability), leading to limited content validity and responsiveness to change [4, 17]. The GIS showed poor construct validity, with low correlations between the subscales of GIS (except unmet treatment need) and physician-rated severity ($r=0.02$ – 0.34), although moderate correlations were seen with patient-rated severity ($r=0.31$ – 0.45) [7, 19]. Correlations of the SF-36 Mental Component Summary (MCS) ($r=-0.17$ to -0.43) with the GIS were generally higher than those seen with the Physical Component Summary (PCS) ($r=-0.10$ to -0.20) (NB correlation coefficients are negative, as higher scores indicate better health status on the SF-36 but worse health status on the GIS [5]). The GAQ 1.0 had better correlation with the MOS health distress questionnaire ($r=0.03$ – 0.46) than the SF-36 (PCS, $r=0.02$ – 0.34 ; MCS, $r=-0.01$ to 0.23) [6]. The HAQ-DI and HAQ II correlated with each other ($r=0.87$) as well as the SF-36 (HAQ-DI, $r=-0.41$ to -0.67 ; HAQ II, $r=-0.35$ to 0.72) [15, 18]. Most instruments had good or excellent internal consistency (Cronbach's $\alpha=0.4$ – 1.0), except the GIS (weak correlation between items of the gout medication side effects and unmet treatment needs) [7]. Test-retest reliability was low for the AIMS [intraclass correlation coefficient (ICC)= 0.11 – 0.70] and the MOS 20 (ICC= 0.27 – 0.65) [16] but acceptable for the HAQ-DI (ICC= 0.68 – 0.84) [15]. Responsiveness to clinical change was elicited by the Minimal Clinically Important Difference (MCID) of 5–8 points for the subscales of the GIS [19], SF-36 [17] and GAQ 1.0 (in all subscales except well-being anchored to pain frequency) [6] and a 20% change in scores of the AIMS and MOS 20 [16]. Effect sizes (ESs) of the PCS (SF-36) improved from small (0.3) in the treatment with colchicine only to large (0.99) in the urate lowering treatment (ULT) and colchicine group [17]. The magnitude of the ES was lower for the GIS (0.218–0.376 in the minimally improved and 0.129–0.682 in the markedly improved groups) [19] and moderate (0.62) for the HAQ-DI [15].

The distribution of HRQOL in gout

No studies were identified that defined or used a cut-off value for poor HRQOL in gout. Higher scores indicate worse HRQOL in the GIS, GAQ 1.0, HAQ-DI, AIMS and BIPQ and better HRQOL in the WHOQOL-BREF, SF-36 including PF10, MOS 20 and SF-12v2. Four studies identified instruments with scores lower than controls (SF-36 physical functioning, role physical, bodily pain, general health, role emotional, PCS $P<0.001$ [20]; WHOQOL-BREF $P=0.003$ [21]) and USA normative distribution (SF-36 PCS $P=0.007$ [22], $P<0.001$ [30]), representative

TABLE 1 Characteristics of studies providing data on HRQOL in gout

Reference	Study period	Publication year	Location	Source of data/recruitment	Study type	Sample size	Questionnaire to measure HRQOL
Singh and Strand [20]	1996–98	2008	USA	Veterans Affairs database	Cross-sectional	70334	SF-36 (veterans)
Colwell <i>et al.</i> [6]	NR	2006	USA	Phase 2 clinical trial of febuxostat	Nested prospective cohort	126	GAQ 1.0
Taylor <i>et al.</i> [4]	NR	2008	New Zealand	Study of hand function in gout and rheumatology clinics	Cross-sectional	73	HAQ-DI
Hirsch <i>et al.</i> [24]	NR	2010	USA	Multispecialty clinics (physician, poster and newspaper advertisement recruitment)	Cross-sectional	371	GIS
Hirsch <i>et al.</i> [7]	NR	2008	USA	Multispecialty clinics (physician, poster and newspaper advertisement recruitment)	Cross-sectional	371	GIS
Roddy <i>et al.</i> [21]	NR	2007	UK	Two GP practices	Cross-sectional	13684	WHOQOL-BREF
Dalbeth <i>et al.</i> [25]	NR	2011	New Zealand	Advertisements in the community and secondary care clinics	Prospective cohort	142	BIPQ, HAQ II
Alvarez-Hernandez <i>et al.</i> [16]	NR	2009	Spain	Not described	Prospective cohort	49	AIMS, MOS 20
Lee <i>et al.</i> [22]	NR	2009	USA	Advertisements in primary and secondary care clinics	Cross-sectional	371	SF-36
Sarkin <i>et al.</i> [26]	NR	2010	USA	Advertisements in community clinics and newspapers	Cross-sectional	260	GIS
Becker <i>et al.</i> [33]	NR	2009	USA	Academic and private rheumatology clinics	Prospective cohort	110	SF-36 and HAQ-DI
ten Klooster <i>et al.</i> [18]	2005–08	2011	Netherlands	Outpatient rheumatology clinics	Cross-sectional	102	HAQ-DI, HAQ II and SF-36 PF10
Khanna <i>et al.</i> [23]	NR	2008	USA	Private clinic and University of Cincinnati Veterans Affairs Medical Center	Cross-sectional	80	SF-36, EQ5D and HAQ-DI
Alvarez-Hernandez <i>et al.</i> [15]	NR	2008	Mexico	Eight rheumatology departments	Prospective cohort	206	HAQ-DI
Khanna <i>et al.</i> [17]	NR	2011	Spain	Gout clinic	Prospective cohort	99	SF-36
Lindsay <i>et al.</i> [31]	NR	2011	New Zealand	Primary and secondary care clinics	Qualitative interviews	11	None
Khanna <i>et al.</i> [19]	NR	2011	USA	RCT of rilonocept vs placebo	Nested prospective cohort	73	GIS
van Groen <i>et al.</i> [27]	2005–08	2010	Netherlands	Outpatient rheumatology clinic	Cross-sectional	102	HAQ-DI
Alvarez-Nemegyei <i>et al.</i> [28]	1999	2005	Mexico	Primary care	Nested case-control in a cohort	90	HAQ
Harrold <i>et al.</i> [32]	2005–10	2010	USA	Multispecialty practice (Fallon clinic)	Qualitative	26	None
Singh <i>et al.</i> [29]	NR	2011	USA	Multispecialty clinics (physician, poster and newspaper advert recruitment)	Cross-sectional	298	Healthcare utilization frequency
Khanna <i>et al.</i> [30]	2010	2012	USA, UK, Germany, France	National Health and Wellness Survey, Lightspeed Research panel	Cross-sectional	1936	SF-12v2, SF-6D

NR: not reported; RCT: randomized controlled trial.

TABLE 2 Modified NOS quality assessment for cross-sectional and cohort studies

Study details	Selection			Comparability		Assessment of HRQOL in addition to self-reported data			
	Cohort representative of average gout patient in community	Controls from same source as cases	HRQOL associations (CS) or predictors/ change (Cht)	Diagnosis of gout: MSU crystals, ARA criteria (35) or record linkage	Controls matched for age/ gender	Measure of association between gout and HRQOL (OR or RR)	Independent physician assessment, secure records or record linkage	Adequate follow-up period (Cht only)	Response rate >60% (CS) or attrition <30% (Cht)
CS									
Singh and Strand [20]	+	+	+	+	—	NR	+	Not relevant	—
Hirsch <i>et al.</i> [24]	+	NR	+	+	NR	NR	+	Not relevant	+
Hirsch <i>et al.</i> [7]	+	NR	+	+	NR	NR	+	Not relevant	+
Roddy <i>et al.</i> [21]	—	+	+	—	—	NR	+	Not relevant	—
Lee <i>et al.</i> [22]	+	NR	+	+	NR	NR	+	Not relevant	+
Sarkin <i>et al.</i> [26]	+	NR	+	+	NR	NR	+	Not relevant	NR
ten Klooster <i>et al.</i> [18]	—	NR	+	+	NR	NR	—	Not relevant	+
Khanna <i>et al.</i> [23]	+	NR	+	+	NR	NR	+	Not relevant	NR
Taylor <i>et al.</i> [4]	—	NR	+	+	NR	NR	—	Not relevant	NR
van Groen <i>et al.</i> [27]	—	+	NR	+	—	NR	—	Not relevant	NR
Alvarez-Nemegyei <i>et al.</i> [28]	+	+	+	+	—	NR	—	Not relevant	NR
Singh <i>et al.</i> [29]	+	NR	+	+	NR	NR	+	Not relevant	NR
Khanna <i>et al.</i> [30]	+	NR	+	—	NR	NR	—	Not relevant	+
Cht									—
Colwell <i>et al.</i> [6]	—	NR	+	—	NR	NR	+	+	+
Dalbeth <i>et al.</i> [25]	+	NR	+	+	NR	NR	+	+	+
Alvarez-Hernández <i>et al.</i> [16]	—	NR	+	+	NR	NR	+	—	+
Becker <i>et al.</i> [33]	—	NR	+	+	NR	NR	+	+	—
Alvarez-Hernández <i>et al.</i> [15]	+	NR	+	+	NR	NR	+	+	+
Khanna <i>et al.</i> [17]	—	NR	+	+	NR	NR	+	+	—
Khanna <i>et al.</i> [19]	—	NR	+	—	NR	NR	—	—	+

+: positive rating; —: negative rating; Cht: cohort study; CS: cross-sectional study; MSU: monosodium urate; NR: not reported; RR: relative risk.

TABLE 3 Measurement values of instruments used to measure HRQOL

Measurement instrument	Reliability		Validity		Scale development		Responsiveness
	Internal consistency (Cronbach's α)	Test-retest (ICC)	Content	Construct (Pearson or Spearman's r)	Concurrent (Pearson or Spearman's r)	Hypothesis <i>a priori</i>	
GIS [7, 19]	0.54–0.94	0.77–0.89	Patients and rheumatologists	Patient severity ($r = 0.31$ – 0.45), attack freq. ($r = 0.06$ – 0.51), attack pain ($r = 0.13$ – 0.47), physician severity ($r = 0.02$ – 0.34), PCS ($r = -0.10$ to -0.20), MCS ($r = -0.17$ to -0.43)	NR	Yes	ES 0.218–0.376 in the minimally improved and 0.129–0.682 in the markedly improved groups
GAQ 1.0 [6]	0.78–0.97	NR	Patients and Rheumatologists	PCS ($r = 0.02$ – 0.34), MCS ($r = -0.01$ to 0.23), MOS ($r = 0.03$ – 0.46)	NR	Yes	GRR 0.030 (1 month) to 1.142 (6 months), MCID 1.88–12.33 (not significant in well-being for pain freq.)
HAQ-DI [4, 15, 18, 33]	0.81–0.97	0.68–0.84	Floor 20.5%, Ceiling 34%	Freq. of flares ($r = 0.41$), physician global ($r = 0.42$ – 0.77), swollen joints ($r = 0.40$ – 0.62), painful joints ($r = 0.46$ – 0.650), joints with limited mobility ($r = 0.36$), VAS pain ($r = 0.56$), tophi ($r = 0.42$), excellent/very good health = 0.16, good = 0.33, fair/poor = 1.25	SF-36 ($r = -0.41$ to -0.67), PCS ($r = -0.71$), MCS ($r = -0.56$), DASH ($r = 0.81$), Sollerman ($r = -0.79$), ACR functional class ($r = 0.79$), HAQ II ($r = 0.87$), PF 10 ($r = -0.75$)	Yes (55.5% true)	Mean ES = 0.62 (moderate), SDC = 0.59 and GRR = 1.91
SF-36 [17, 33]	0.75–0.97	0.40–0.90	Ceiling RP = 18.4%, SF = 32.7%, RE = 58.6%	PCS: tophi ($r = 0.277$), swollen joints ($r = -0.334$), painful joints ($r = -0.544$), flares last year ($r = -0.369$); MCS: painful joints ($r = -0.436$), freq. of flares ($r = -0.321$)	NR	NR	Colchicine: ES for PCS = 0.3 (small), ES for MCS = 0.16 (negligible) Colchicine + ULT: ES for PCS = 0.99 (large) ES for MCS = 0.08 (negligible), MCID (all subjects) 70% for PCS and 38% in MCS
MOS 20 [16]	0.68–1.0	0.27–0.65	NR	JFL: 23.75–66 Without JFL: 37.59–81.43	HAQ-DI ($r = -0.1$ to -0.5)	NR	>20% change: PF, SF, health perception, pain
AIMS [16]	0.66–0.96	0.11–0.70	NR	JFL: 3.05–6.62 Without JFL: 1.99–5.46	HAQ-DI ($r = 0.1$ – 0.6)	NR	>20% change: dexterity, daily activity, social development, pain, depression
HAQ II [18]	0.94	NR	Ceiling 25.8%	Excellent/very good health = 0.28, good = 0.44, fair/poor = 1.39	PF 10 ($r = -0.79$), SF-36 [-0.35 (MH) to 0.72 (RP)]	Yes	NR
PF 10 [18]	0.94	NR	NR	Excellent/very good health = 71.91, good = 74.27, fair/poor = 39.33	HAQ-DI ($r = -0.75$), SF-36 [0.30 (MH)–0.68 (RP)]	Yes	NR

SDC: smallest detectable change; GRR: Guyatt's responsiveness ratio; NR: not reported; JFL: joints with functional limitations; SF-36 subscales: RP, role physical; MH, mental health; SF, social function; RE, role emotional; freq.: frequency.

of poor HRQOL in gout. One cohort study of treatment-failure gout showed lower scores in all SF-36 domains (except mental health and MCS) compared with age- and sex-matched US normative distributions (PCS and MCS normative distributions have a mean of 50 and a standard deviation of 10 for the US population) [33]. One cohort [17] and two cross-sectional studies [21, 22] highlighted the greater impact of gout on physical HRQOL as measured by the SF-36 [17] and WHOQOL-BREF ($P < 0.001$) [21], with a lesser reduction seen in the MCS compared with US norms ($P < 0.001$) [22]. However, the impact on physical function was mild, as shown in two studies using the HAQ-DI, with a baseline HAQ-DI of 1 for those with treatment-failure gout [33] and 0.43 in chronic tophaceous gout [16]. (Consensus-based cut-off for mild disability as measured by the HAQ-DI is a score < 1 , moderate disability 1–2 and severe disability ≥ 2 [36].) Similarly the average HAQ score (surrogate for musculoskeletal disability) in another study was 0.17 [28]. Two cross-sectional studies [27, 30] comparing the impact of gout with that of other rheumatic diseases showed substantially lower levels of disability (mean HAQ-DI 0.54) in patients with gout compared with those with RA (0.97) and OA (1.00) [27]. Those with severe gout (three or more flares in the previous year and confirmed tophi) had similar health utility (SF-6D) scores as patients with average RA or systemic lupus [36]. In two studies that utilized the GIS, participants' gout concern remained high despite their reporting that they found treatment helpful [19, 24], and in another cohort study using the generic BIPQ, the impact of gout was most severe on perceptions of chronicity [25]. Gout severity was also associated with an increased utilization of primary care clinics in a cross-sectional study of health care resources utilization ($P = 0.005$) [29].

Factors associated with poor HRQOL in gout

Two studies of physical functioning (measured by the SF-36 and HAQ-DI) as a surrogate marker of HRQOL and another study of health care utilization found that associated comorbidities contribute to poorer HRQOL (PCS, $r = -0.18$ to -0.43 , $P < 0.01$ [22]; HAQ-DI, $P < 0.03$ [33]) and a greater number of primary care visits ($P = 0.006$) [29]. In one study of US veterans, comorbidities were solely responsible for poor HRQOL, with no difference in HRQOL between those with and without gout after comorbidities had been adjusted for [20]. However, in one cross-sectional study the association between gout and poor physical HRQOL of the WHOQOL-BREF remained significant after adjustment for medical (diabetes, hypertension and chronic kidney disease) and musculoskeletal comorbidities (WHOQOL-BREF, $P = 0.001$ [21]). Cross-sectional association of gout characteristics [presence of tophi (PCS, $P < 0.01$; MCS, $P < 0.05$), uncertainty about the presence of tophi (PCS, $P < 0.001$; MCS, $P < 0.01$) and four or more flares in the last 12 months (PCS, $P < 0.05$; MCS, $P < 0.05$)] with poor HRQOL and high activity impairment also remained significant even after adjustment for comorbidities [30]. In one cohort

[25] and four cross-sectional studies [7, 22, 28, 30], gout-specific features, including increasing frequency of flares ($P = 0.002$ [22], $P = 0.044$ [25], $r = 0.51$ [7], $P < 0.05$ [30]), time with pain between attacks ($P < 0.001$ [22]), pain during a typical attack ($P = 0.023$ [22]), number of joints involved in a typical attack ($P = 0.004$ [22]) and presence of tophi {relative risk (RR) = 4.3, 95% confidence interval (CI) 1.2, 15.1 [28], $P < 0.05$ [30]} were reported to be associated with worse HRQOL (measured by the GIS, SF-36, SF-12v2, HAQ and BIPQ) even after adjustment for age, gender, gout features and comorbidities. Increased frequency of flares in the previous year (three or more) (PCS, $P < 0.05$) and confirmed tophi (severe gout) (PCS, $P < 0.01$; MCS, $P < 0.01$) led to worse HRQOL compared with asymptomatic patients [30]. The presence of tophi had a significant impact on activity impairment ($P < 0.05$ [30]) and led to an increased likelihood of consultation with a rheumatologist {odds ratio (OR) = 7.92, 95% CI 2.81, 22.34, $P < 0.0001$ [29]} in two cross-sectional studies [29, 30]. Other cross-sectional variables such as physician-rated severity (primary care OR = 1.46, 95% CI 1.02, 2.08, $P = 0.037$; rheumatologist OR = 1.52, 95% CI 1.08, 2.14, $P = 0.018$), time since last gout attack (primary care OR = 0.65, 95% CI 0.55, 0.76, $P < 0.0001$; rheumatologist OR = 0.78, 95% CI 0.67, 0.91, $P = 0.001$) and an attack within the last 3 months (primary care OR = 3.48, 95% CI 1.84, 6.58, $P < 0.0001$; rheumatologist OR = 2.11, 95% CI 1.22, 3.65, $P = 0.008$) were also associated with health care resources utilization [29]. While some studies support the association of tophi (GIS, $P = 0.029$ [24]; PCS, $P < 0.01$; MCS, $P < 0.05$ [30]) and serum uric acid (SUA) ($P = 0.002$) [25] with poor HRQOL, others do not (tophi: patient-severity rating, $r = 0.174$ [26]; SUA: WHOQOL-BREF, $P = 0.750$ [21]; GIS, $r < 0.29$ [24]; patient-severity rating, $r = 0.06$ [26]). There was a paucity of cross-sectional evidence for positive effects of allopurinol on HRQOL from a patient's perspective (WHOQOL-BREF, $P = 0.618$ [21]; HAQ, $P = 0.79$ [28]), whereas steroid and non-steroidal anti-inflammatory drugs were associated with greater musculoskeletal disability [28]. Although tophi, comorbidities, polyarticular disease and radiographic damage were associated with worse HRQOL at baseline, after multivariate analysis, a reduction in flares ($P = 0.001$ – 0.06) and baseline SUA ($P = 0.001$ – 0.04) were predictors of improvement in HRQOL in one cohort study [17].

Discussion

Although none of the identified instruments to measure HRQOL in gout in this review were satisfactory in all domains of the assessed clinimetric properties, generic instruments (HAQ-DI, SF-36) received the highest ratings. Correlations with clinical characteristics, other instruments and change in scores coupled with clinical change strengthened their construct and concurrent validity as well as responsiveness. The SF-36 and HAQ-DI have been endorsed by the OMERACT group as validated tools to measure HRQOL and functional disability in gout [37, 38]. While the generic instruments allow

comparison between the impact of different diseases, their treatments and cost-effectiveness analyses, they may lack the sensitivity to capture the true impact of gout, especially in those with less severe disease [39]. The disease-specific GIS may focus on HRQOL domains more relevant in gout (hence a better correlation with patient-reported factors) and be more responsive to small changes in health status [40]. However, it may miss any unexpected adverse outcomes and does not allow comparison between disease states. Furthermore, the OMERACT group has not yet unreservedly endorsed the Gout Assessment Questionnaire 2.0 and its GIS subscale as fully validated HRQOL measures in chronic gout [38].

A consistent finding of all the instruments reviewed is that people with gout had lower physical HRQOL compared with the normative distribution [20, 22] as well as study controls [21], even after adjusting for comorbidities [7, 22, 24]. This may be due to the strong emphasis on physical functioning as a surrogate measure for HRQOL in the generic instruments. The impact of SUA and tophi were variable, with some studies reporting an adverse effect on HRQOL [17, 24] but others showing no effect [21, 26]. SUA may have an indirect relationship with HRQOL in gout, as it is positively correlated with the frequency of flares in the last 12 months as well development of tophi [28, 30, 41]. Although allopurinol is not perceived by patients to improve HRQOL [21, 28], its use in primary care is often suboptimal [42] and it has been shown to reduce the number of flares as well as tophi [43, 44]. Patients may be unaware of the rationale behind ULT, with many discontinuing treatment at the onset of flares when ULT is initiated [32].

The robustness of the findings of this review is supported by data extraction and quality assessment using validated tools by two independent reviewers. Our search strategy included a filter that is 90–97% sensitive in retrieving clinimetric articles [12], therefore it is unlikely that we would have missed any such articles. Nevertheless, the findings of the review need to be interpreted in the context of the limitations of the study design as well as those of the literature identified. A limitation is that the articles included in the review were restricted to English (due to a lack of translation facilities) as well as not searching for grey literature (presumed low yield). The generalizability of the results may be limited by the highly selective populations studied (treatment failure or chronic tophaceous gout in the intercritical stage, mainly Caucasian males), study settings (private or specialist clinics) and variable response rates.

Existing studies of HRQOL in gout are limited by their paucity of longitudinal data, recruitment from highly selective secondary care populations and use of mostly generic instruments to measure HRQOL. Hence there is a need for a primary care-based prospective cohort study using both gout-specific and generic questionnaires to determine how HRQOL changes over time in the clinical setting, where most patients with gout are treated, identify which factors (such as disease characteristics, treatment, comorbidities including anxiety and depression) predict

changes in HRQOL and also identify those at risk of deterioration to better target their treatment.

Rheumatology key messages

- Existing studies of gout most commonly use generic measures of HRQOL.
- Gout is associated with poorer physical HRQOL.
- Poor HRQOL in gout is associated with both disease-specific characteristics and comorbidity.

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Supplementary data

Supplementary data are available at *Rheumatology* Online.

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Appendix 2: Prospective observational cohort study of Health Related Quality of Life (HRQOL), chronic foot problems and their determinants in gout: a research protocol.

STUDY PROTOCOL

Open Access

Prospective observational cohort study of Health Related Quality of Life (HRQOL), chronic foot problems and their determinants in gout: a research protocol

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Abstract

Background: Gout is the commonest inflammatory arthritis affecting around 1.4% of adults in Europe. It is predominantly managed in primary care and classically affects the joints of the foot, particularly the first metatarsophalangeal joint. Gout related factors (including disease characteristics and treatment) as well as comorbid chronic disease are associated with poor Health Related Quality of Life (HRQOL) yet to date there is limited evidence concerning gout in a community setting. Existing epidemiological studies are limited by their cross-sectional design, selection of secondary care patients with atypical disease and the use of generic tools to measure HRQOL. This 3 year primary care-based prospective observational cohort study will describe the spectrum of HRQOL in community dwelling patients with gout, associated factors, predictors of poor outcome, and prevalence and incidence of foot problems in gout patients.

Methods: Adults aged ≥ 18 years diagnosed with gout or prescribed colchicine or allopurinol in the preceding 2 years will be identified through Read codes and mailed a series of self-completion postal questionnaires over a 3-year period. Consenting participants will have their general practice medical records reviewed.

Discussion: This is the first prospective cohort study of HRQOL in patients with gout in primary care in the UK. The combination of survey data and medical record review will allow an in-depth understanding of factors that are associated with and lead to poor HRQOL and foot problems in gout. Identification of these factors will improve the management of this prevalent, yet under-treated, condition in primary care.

Keywords: Gout, HRQOL, Foot, Patient experience, Prospective cohort, Primary care

Background

Gout is the most prevalent inflammatory arthropathy, affecting around 1.4% of the adult population in the UK [1]. It is caused by monosodium urate (MSU) crystal deposition in and around joints once the physiological saturation threshold in body tissues for uric acid is exceeded. The most commonly affected joints are the first metatarsophalangeal joint (1st MTPJ), mid foot and

ankle. The first acute attack affects the 1st MTPJ in 56-78% of the patients with 90% having acute gout of the great toe at some point in their disease course [2] yet chronic foot problems are also common in people with gout. Hallux valgus deformity and chronic pain in the great toe are more common in people with gout than age and gender-matched controls [3]. A small hospital-based study has shown more frequent gait impairment and foot-related functional problems in patients with gout than in those without [4]. There is little evidence from a primary care perspective about the potential long-term consequences of gout for the foot.

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Gout also has an adverse impact on patients' health related quality of life (HRQOL) [5,6] and emotional, social and physical functioning, resulting in significant disability. Factors directly related to gout symptoms such as frequency and severity of acute attacks as well as those related to disease complications and adverse effects of gout treatment, all potentially contribute to impaired HRQOL. Cross-sectional epidemiological studies in primary care have shown that gout has an independent association with impaired HRQOL, particularly affecting the physical domain, after adjustments for co-morbidities such as osteoarthritis, renal and cardiovascular disease [6,7]. 'Treatment failure' gout within a hospital-based cohort has also been found to have a significant impact on patient HRQOL and disability, especially in the realm of physical functioning [5]. The same cohort study demonstrated that the patients' perception of disease severity correlated more closely with HRQOL than the physicians' assessment of disease severity. Patients and healthcare providers often have different perspectives of what constitutes optimal management of gout [8]. Whilst physicians regard pharmacological treatment of gout to be effective, most patients discontinued treatment due to adverse or no positive effects, treatment-induced flares and financial constraints [8]. A recent qualitative study [9] on the impact of gout highlighted the lack of understanding and the stigma associated with this condition which often leads to under-reporting of symptoms. This in turn can lead to suboptimal treatment despite disease severity.

These findings are not surprising given that, until recently, there has been little published work on the implications of gout in terms of morbidity and mortality as well as associated healthcare utilisation and costs [10]. The majority of gout is managed within the primary care setting, yet most of the research to date has taken place in secondary care which may deal with more complex and atypical presentations including those who have failed to respond to or not tolerated standard therapies. Therefore the applicability of such data is questionable in the wider community setting. Existing epidemiological studies have had limitations such as small sample size, cross-sectional design and the use of generic rather than disease-specific instruments such as the Gout Impact Scale (GIS) to measure HRQOL [11]. Little is known about the changes in HRQOL in gout patients due to the lack of longitudinal follow-up.

Hence there is a need for a prospective observational cohort study in primary care which incorporates patient-reported outcomes (PRO) to assess long-term outcome and consequences of gout, focusing particularly on HRQOL and foot problems. Improving understanding of which factors predict outcome would help substantiate indications for urate-lowering therapy (ULT) and identification of patients at which this should be targeted

Objectives of the study

1. To describe the spectrum of HRQOL in patients with gout and its distribution by demographic, socio-economic and anthropometric characteristics.
2. To describe the prevalence, onset, persistence and progression of chronic foot problems in gout over 3 years.
3. To examine:
 - a) Cross-sectional associations between poor HRQOL and gout disease characteristics and treatment, chronic foot problems, co-morbidities, and psychosocial factors in gout.
 - b) Change in HRQOL in gout over 3 years and determine which of the associated factors may predict deterioration or recovery.

Methods

Design

A primary care-based prospective cohort study with linked medical record review. All phases of the study have been approved by the North West-Liverpool East Research Ethics Committee (Reference number 12/NW/0297).

Sampling frame

Inclusion criteria

- Aged >18 years.
- Registered with 30 general practices in the West Midlands, UK.
- Read code consultation for gout or a prescription for colchicine or allopurinol during the preceding two years.

Exclusion criteria

- Under 18 years of age.
- Vulnerable groups – e.g. significant cognitive impairment, severe enduring mental illness, active malignancy or other terminal illness.
- Those who are unable to complete the questionnaires in English.

Data collection time points

The different phases of the study are illustrated in Figure 1.

Phase 1: baseline postal questionnaire survey

Patient identification Staff from the West Midlands North Primary Care Research (WMN PCR) will conduct a single electronic search of the primary care records in participating practices to identify patients with Read codes for a consultation for gout or a prescription for

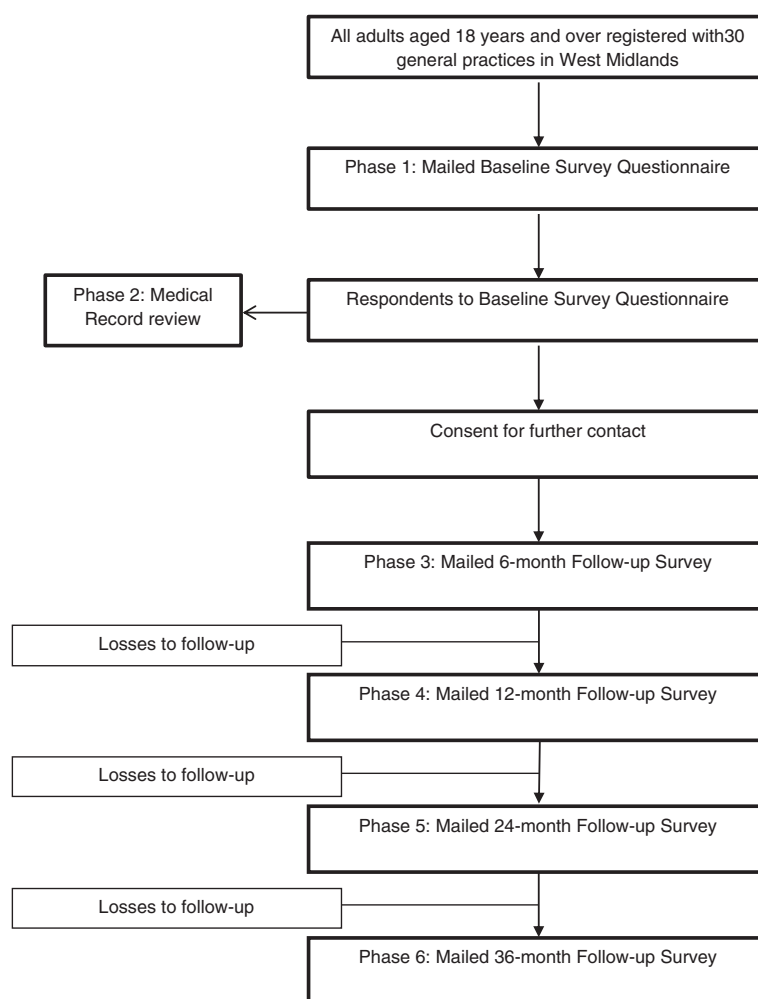


Figure 1 Flowchart of study procedure.

colchicine or allopurinol within the last two years. The Read codes used by the Arthritis Research UK Primary Care Centre (ARUKPCC) to define gout are listed in Table 1. The WMN PCR team members will screen the mailing lists (prior to mailing) for patient deaths and departures from the practice to ensure that patients are

not inappropriately contacted. The lead general practitioner (GP) at each practice will be invited to identify potentially vulnerable patients to be excluded.

Table 1 Read Codes used to identify consultations with gout in primary care

Code	Term
C34	Gout
N023	Gouty arthritis
EGTON 227	Gout NOS
OX2740G	Gout Acute/ox
1443	H/O: gout
EMISR4QG01	Gouty tophi + Gout NOS
2D52	O/E - auricle of ear - tophi
669	Gout monitoring

Initiating patient contact All eligible patients will be sent a study pack from their GP containing a letter of invitation, participant information sheet (PIS), a pre-paid return envelope and a baseline self-completion questionnaire which will also include a consent form asking for consent for further contact and review of their medical records. Potential participants will be provided with a contact name and telephone number should they have any queries about the study. Patients will be informed that they are under no obligation to participate and that if they decline their normal clinical care will not be affected in any way. Participants will be asked to return completed questionnaires, and upon receipt by the research centre, the response will be recorded against a unique patient number in a mailing database.

Non-responders to mailed baseline study pack After two weeks, those who have not responded will be sent a reminder postcard from their GP. After a further two weeks, a reminder letter with repeat baseline questionnaire will be sent to those who have yet to respond (4 weeks after the first questionnaire). Those who fail to respond after all three baseline mailings will be assumed not to have consented to the study and will not be contacted again.

The questionnaire The questionnaire will be divided into 7 main sections

- a) Gout symptoms and treatment.
- b) The impact of gout on daily life.
- c) General health (including co-morbidities and measures of physical function).
- d) Measures of anxiety and depression.
- e) Foot and other joint problems.
- f) Occupational characteristics.
- g) Socio-economic and demographic characteristics.

Details of the conceptual domains, operational definitions and empirical measures are provided in Table 2. The completed baseline questionnaires will have the responses securely stored in the study database.

Data entry, coding, cleaning and storage A specific study database will be created to record responses to the questions. Data entry will be performed by dedicated trained members of the administrative team as the completed questionnaires are returned. Although they are experienced in data entry, specific training will be provided for this study. The principal investigator (PI) and study statistician will determine coding prior to data entry into the database which will provide coding options. One in ten random questionnaires will be checked by a member of the study team for the purposes of quality assurance. This information is kept by the research support co-ordinator. Only relevant members of the research team will have access to the database which is password protected. Requests for access to the data stored in this database must be made in writing, along with an analysis plan, to the Chief Investigator (CI). Questionnaires and consent sheets are securely stored in separate locations to protect patient confidentiality.

Phase 2: Review of general practice medical records

All participants in Phase 1 who give permission for their GP records to be accessed will have their computerised medical records tagged by a member of the WMN PCR team. The practices participating in this study are fully computerised and undergo annual audits completed by the WMN PCR team to assess the quality

and completeness of the data at the practices [23]. All consultations for the 2 years prior to study entry and then prospectively for the three-year study period will be identified. The data obtained will include co-morbidities, repeat consultations for gout, prescription patterns and referral to secondary care. All patient identifiable data (name, contact details) will be removed from the medical records and the consultation data will be linked to the survey data by unique survey identifier.

Phase 3, 4, 5 and 6: Follow-up at 6, 12, 24 and 36 months

Follow-up surveys will be mailed at 6, 12, 24 and 36 months to all participants in phase 1 who consented to further contact. The focus of follow-up will be clinical (pain/disability severity) change and the possible determinants of this. The questionnaire will include repeated measures of general health (including generic measures of physical function), psychosocial factors, co-morbidity and gout symptoms. Non-responders to the questionnaire will be sent a reminder postcard after two weeks. Those who do not respond to the reminder postcard will be sent a repeat questionnaire, PIS and a further covering letter four weeks after the initial mailing. The WMN PCR team members will screen the mailing lists (prior to mailing) for patient deaths and departures from the practice to ensure that patients are not inappropriately contacted.

Sample size Disease specific HRQOL scores will be recorded using the Gout Impact Scale at baseline, 6, 12, 24 and 36 months. In order to use the information recorded at all five points, a sample size of 882 would allow a smallest meaningful difference in HRQOL of 0.2 standard deviation units to be detected between two groups (441 subjects per group) defined in terms of frequency of gout attacks (<2 attacks, ≥2 attacks per year) using a linear mixed model (significance 0.05, power 90%, autocorrelation 0.8) [24]. Allowing for 70% response at baseline and 30% drop out over the follow-up period would require 1800 people with gout to be contacted at baseline.

Statistical analysis

Baseline

Descriptive statistics will be used to assess response bias, along with the characteristics of the baseline population.

Factors associated with levels of HRQOL at baseline will be assessed using students' t-tests chi-squared tests, and logistic regression, as appropriate.

Follow-up Descriptive statistics will be used to assess attrition bias and to describe the onset, and persistence of foot problems and their characteristics.

Table 2 Questionnaire items

Conceptual domain	Operational definition	Empirical measure	Number of items	Time point
Section A: About Gout				
Gout frequency	No. of attacks in the last 12 months/since last contact	Numerical rating scale 0- \geq 5	1	All
Age at diagnosis	Age in years	Numerical free text box	1	BL
Acute attack of gout	Acute episode at time of questionnaire	Yes/No	1	All
Allopurinol	Reported use of allopurinol	Yes/No	1	All
	Current daily dose of allopurinol	Nine daily dose options: 50 mg-900 mg	1	All
Section B: How gout affects your life				
Gout concern, wellbeing, productivity, convenience and satisfaction	Gout Impact Scale [11]	5-item Likert scale	18	All
Illness perception	Modified Illness perception questionnaire [12]	5-item Likert scale	4	BL, 12 months, 36 months
Section C: General Health				
Physical function	SF36 Physical function sub-scale (PF10) [13]	3-item Likert scale	10	All
	Health Assessment Questionnaire Disability Index [14]	4-item Likert scale	17	All
Co-morbidities	Diabetes mellitus, Renal failure, renal calculi, Cerebrovascular accident, Transient ischaemic attacks, ischaemic heart disease, hyperlipidaemia	Yes/No	9	BL
Section D: How you feel				
Depression	Patient health questionnaire (PHQ 9) [15]	4 point Likert scale	16	BL, 12 months, 36 months
Anxiety	Generalised anxiety disorder questionnaire (GAD) [16]			
Section E: Foot and other joint problems				
Hallux valgus	Self-completed line drawings [17]	5 line-drawings for each foot depicting increasing severity of hallux valgus	2	BL, 12 months, 36 months
Pain	Pain in the hands, hips, knees and feet in the last year	Yes/No	4	BL, 12 months, 36 months
	Location of body pain in last 4 weeks	Self-completed body manikin [18,19]	1	BL, 12 months, 36 months
Foot pain	Foot pain, aching, stiffness in last month [20]	Frequency on 5-point Likert scale	1	BL, 12 months, 36 months
Foot pain location	Location of foot pain in last four weeks	Self-completed foot manikin [21]	1	BL, 12 months, 36 months
Foot function	Manchester Foot Pain and Disability Index [22]	Frequency on 3-point likert scale	17	BL, 12 months, 36 months
Consultation for foot problems	Consultation with GP, physiotherapy, podiatry, in last 12 months/since last contact	Yes/No	4	BL, 12 months, 36 months
Section F: Work				
Occupational characteristics	Current employment status	11-response options	1	BL, 12 months, 36 months
	Work absence during last 6 months due to joint/back problems	Yes/No	1	BL, 12 months, 36 months
	Ability to do usual job	5-response options	1	BL, 12 months, 36 months
Section G: Demographic/socioeconomic characteristics				
Date of birth	Date of birth	Date of birth	1	BL

Table 2 Questionnaire items (Continued)

Gender	Gender	Male/Female	1	BL
Anthropometric characteristics	Height	Meters or feet/inches	1	All
	Weight	Kilogram or stones/pounds	1	All
Marital status	Marital status	6-response options	1	BL
Living alone	Living alone	Yes/No	1	BL
Adequacy of income	Adequacy of income	4-response options	1	BL
Education	Higher education	Yes/No	1	BL
Ethnicity	Ethnicity	6-response options	1	BL
Life-style-characteristics	Frequency of alcohol consumption	6-response options	1	BL
	Weekly amount of beer/spirits/wine consumed	Free-text	1	BL
	Smoking status	3-response options	1	BL

Regression models will be used to assess the factors predicting poor HRQOL and chronic foot problems prospectively over three years.

Imputation techniques will be used to account for missing data and loss to follow up, as appropriate.

Discussion

HRQOL is an important yet under-researched outcome measure in chronic gout. To our knowledge this is the first prospective observational cohort of gout patients in primary care in the UK which uses generic as well as gout-specific questionnaires to assess HRQOL. Through follow-up surveys and medical record review, the study investigates the occurrence and frequency of poor HRQOL, factors associated with it at baseline and predictors of poor outcome at follow-up. A limitation of the study is the identification of patients based on a clinical diagnosis of gout (the gold standard of urate crystal identification in synovial aspirate [25] is not mandatory for inclusion into the study). However, a clinical diagnosis based on the rapid onset of pain, erythema and swelling affecting the 1st MTPJ in the context of hyperuricaemia is supported by the European League Against Rheumatism (EULAR) recommendations for the diagnosis of gout [25]. Potential participants will be identified either by a gout-coded primary care consultation or a prescription for allopurinol or colchicine in the study period. Other urate lowering therapies such as febuxostat and uricosuric drugs will not be included in this search strategy as both are infrequently used in UK primary care. Patients taking either drug will be identified by regular consultations. This study ultimately aims to improve the management of gout in primary care through identifying and considering factors associated with and predictive of poor outcome in a patient-centred treatment plan.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

ER and CM conceived the study. All authors participated in the study design. PC, CM and ER drafted the manuscript which was approved by all authors.

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Appendix 3: Gout Study Questionnaire Baseline Questionnaire Booklet

PRIMARY CARE SCIENCES
ARTHRITIS RESEARCH UK PRIMARY CARE CENTRE

Gout Study Questionnaire

Baseline Questionnaire Booklet

REC Reference Number: 12/NW/0297

INSTRUCTIONS FOR THIS QUESTIONNAIRE

Please answer **all** the questions.

The questions can be answered by putting a cross in a box like this: 

or circling a number like this:

3  5 6

Please write in BLOCK CAPITALS where appropriate. **Please complete the consent form on page 22 if you agree to take part in this study, then complete the questionnaire.**

When you have finished please check that you have answered all of the questions and then return the questionnaire in the envelope enclosed. **You do not need a stamp.** Please return the questionnaire in the next two weeks.

The answers you give in the questionnaire will be treated in the strictest confidence.

Whether you take part in this research or not, your right to use health services at your practice or elsewhere will not be affected.

Details about this project are available in the information sheet enclosed. If you would like further information please contact Priyanka Chandratre on **01782 734721**

THANK YOU

SECTION A: ABOUT GOUT

1. How many attacks of gout have you had in the last 12 months?

(Please put a cross in one box only)

0.....	<input type="checkbox"/>	2.....	<input type="checkbox"/>	4.....	<input type="checkbox"/>
1.....	<input type="checkbox"/>	3.....	<input type="checkbox"/>	5 or more..	<input type="checkbox"/>

2. How old were you when you were first diagnosed with gout?

Age Years

3. Are you having an attack of gout at the present?

Yes ☐ No ☐

4. Have you ever had gout in more than one joint at the same time?

Yes ☐ No ☐

5. Do you currently take a tablet called allopurinol for gout?

Yes ☐ No ☐

If yes, please indicate the dose below

50 mg.....	<input type="checkbox"/>	600 mg.....	<input type="checkbox"/>
100 mg.....	<input type="checkbox"/>	700 mg.....	<input type="checkbox"/>
200 mg.....	<input type="checkbox"/>	800 mg.....	<input type="checkbox"/>
300 mg.....	<input type="checkbox"/>	900 mg.....	<input type="checkbox"/>
400 mg.....	<input type="checkbox"/>	Don't know.....	<input type="checkbox"/>
500 mg.....	<input type="checkbox"/>	Other (please specify).....	<input type="text"/>

SECTION B: HOW GOUT AFFECTS YOUR LIFE

1. Please indicate how much you agree or disagree with the statements below
(Please put a cross in one box only for each statement).

	Strongly disagree	Disagree	Uncertain	Agree	Strongly agree
a. I am worried that I will have a gout attack within the next year	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. I am afraid that my gout will get worse over time	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. I worry that I will not be able to continue to enjoy my leisure activities as a result of my gout	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. I feel anxious that my gout will interfere with my future activities	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. I am bothered by the side effects from my gout medications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. I am mad or angry when I experience a gout attack	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. It is difficult to plan ahead for events or activities because I may have a gout attack	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. I feel depressed when I get a gout attack	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. My current medications are effective at treating a gout attack if I get one	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Strongly disagree	Disagree	Uncertain	Agree	Strongly agree
j. I miss planned or important activities when I have a gout attack	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
k. I worry about the long term effects of my gout medications	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
l. My current medications do not work well to prevent gout attacks from happening	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
m. I have control over my gout	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. **During your last gout attack**, how much of the time did you experience the following?

(Please put a cross in one box only for each statement).

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Miss work because of gout symptoms?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Have difficulty working because of gout symptoms?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Have difficulty with recreational or social activities because of your gout symptoms?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Have difficulty with self care such as bathing, feeding , dressing yourself because of gout symptoms?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3. **During your last gout attack**, how much did your symptoms interfere with the following things?

(Please put a cross in one box only for each statement).

	Not a bit	A little bit	Moderately	Quite a bit	Extremely
a. Your mood?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Your ability to move about?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Your sleep?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Your normal work? (including both work outside the home and housework)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Your recreational activities?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Your enjoyment of life?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Your ability to do what you want to do?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. Please indicate how much you agree or disagree with the statements below

(Please put a cross in one box only for each statement).

	Strongly disagree	Disagree	Uncertain	Agree	Strongly agree
a. There is a lot I can do to control my gout	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. What I will do will affect whether my gout gets better or worse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Treatments are effective in controlling gout	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Gout is a serious condition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

SECTION C: ABOUT YOUR GENERAL HEALTH

We are interested in your general health. **Please answer every question.** Some questions may look similar to others but each one is different. Please take the time to read and answer each question carefully by placing a cross in the box of your choice.

1. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?
(Please put a cross in one box on each line)

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Vigorous activities , such as running, lifting heavy objects, participating in strenuous sports	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling or playing golf	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Lifting or carrying groceries	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Climbing several flights of stairs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Climbing one flight of stairs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Bending, kneeling or stooping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Walking more than a mile	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. Walking half a mile	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. Walking one hundred yards	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j. Bathing and dressing yourself	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. Please place a cross in the box which best describes your abilities over the **past one week**.

	Without any difficulty	With some difficulty	With much difficulty	Unable to do
a. Dress yourself including tying shoe-laces and doing buttons?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Shampoo your hair?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Stand up from a chair?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Get in and out of bed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Cut your meat?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Open a milk carton?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Lift a full glass or cup to your mouth?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. Walk outdoors on flat ground?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. Climb up 5 steps?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j. Wash and dry your entire body?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
k. Take a tub bath?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
l. Get on and off the toilet?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
m. Reach and get a 5 pound object such as a bag of sugar from above your head?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Without any difficulty	With some difficulty	With much difficulty	Unable to do
n. Open car doors?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
o. Open jars that have been previously opened?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
p. Bend down and pick up clothing from the floor?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
q. Turn taps on and off?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
r. Run errands and shop?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
s. Get in and out of a car?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
t. Do chores such as vacu- uming or yard work?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

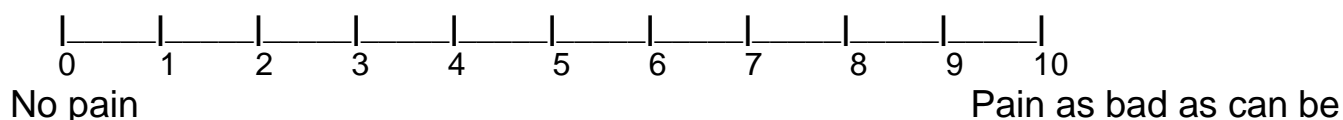
3. Do you use any aids or devices for any of the above activities?
(Please put a cross in as many boxes as apply)

a. Raised toilet seat.....	<input type="checkbox"/>	b. Devices used for dressing (button, hook, zipper pull, shoe horn etc.).....	<input type="checkbox"/>
c. Bathtub bar.....	<input type="checkbox"/>	d. Special or built-up chair....	<input type="checkbox"/>
e. Long-handled appliances for reach.....	<input type="checkbox"/>	f. Built-up or special utensils.....	<input type="checkbox"/>
g. Bathtub seat.....	<input type="checkbox"/>	h. Cane.....	<input type="checkbox"/>
i. Long-handled appliances in bath- room.....	<input type="checkbox"/>	j. Walker.....	<input type="checkbox"/>
k. Jar opener (for jars previously opened).....	<input type="checkbox"/>	l. Crutches.....	<input type="checkbox"/>
m. Wheelchair.....	<input type="checkbox"/>	n. Other (please specify).....	<input type="text"/>

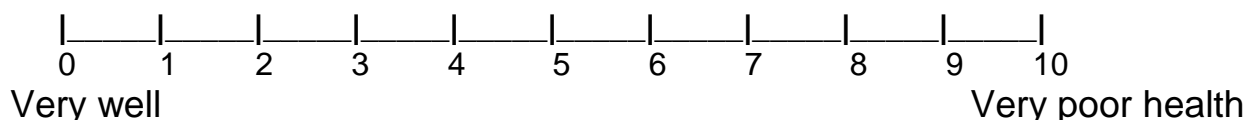
4. Do you receive any help from another person for;
(Please put a cross in as many boxes as apply)

- | | | | |
|--------------------------|--------------------------|-----------------|--------------------------|
| a. Hygiene..... | <input type="checkbox"/> | b. Dressing and | |
| | | Grooming..... | <input type="checkbox"/> |
| c. Gripping and opening | | d. Arising..... | <input type="checkbox"/> |
| things..... | <input type="checkbox"/> | | |
| e. Reach..... | <input type="checkbox"/> | f. Eating..... | <input type="checkbox"/> |
| g. Errands and chores... | <input type="checkbox"/> | h. Walking..... | <input type="checkbox"/> |

5. How much pain have you had in the **past one week**? On a scale of 0 to 10 (where 0 represents “no pain” and 10 represents “pain as bad as can be”), please circle the number below.



6. Please rate how well you are doing on a scale of 0 to 10 (0 represents “very well” and 10 represents “very poor” health).
 Please circle the number below.



7. Have you ever been diagnosed as having or been treated for the following?
(Please put a cross in as many boxes as apply)

- | | | | |
|--|--------------------------|----------------------|--------------------------|
| a. Diabetes..... | <input type="checkbox"/> | b. Stroke..... | <input type="checkbox"/> |
| c. High blood pressure..... | <input type="checkbox"/> | d. TIA or mini | <input type="checkbox"/> |
| | | stroke..... | <input type="checkbox"/> |
| e. High levels of cholesterol, fats or | <input type="checkbox"/> | f. Kidney failure... | <input type="checkbox"/> |
| lipids in your blood..... | | | |
| g. Heart attack..... | <input type="checkbox"/> | h. Kidney stones.. | <input type="checkbox"/> |
| i. Angina..... | <input type="checkbox"/> | | |

SECTION D: ABOUT HOW YOU FEEL

1. The next set of questions are about how you have felt over the last 2 weeks. Please read each item and put a cross in the box that comes closest to how you have been feeling in the **past 2 weeks**.

	Not at all	Several days	More than half the days	Nearly every day
a. Little interest in doing things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Feeling down, depressed, or hopeless	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Trouble falling/staying asleep, sleeping too much	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Feeling tired or having little energy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Poor appetite or overeating	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Feeling bad about yourself, or that you are a failure or have let yourself or your family down	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Trouble concentrating on things, such as reading the newspaper or watching TV	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. Thoughts that you would be better off dead or of hurting yourself in some way	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. If you have been bothered by any of the nine problems above, please answer the following:

How difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

(Please put a cross in one box only)

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3. **Over the last 2 weeks**, how often have you been bothered by any of the following problems?

(Please put a cross in one box only for each statement)

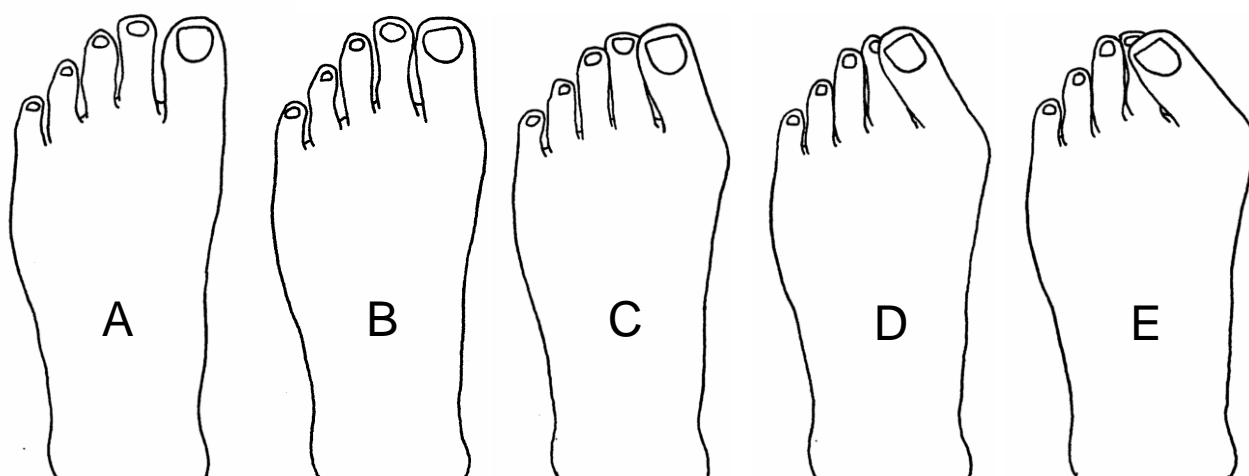
	Not at all	Several days	More than half the days	Nearly every day
a. Feeling afraid that something awful may happen?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Worrying too much about different things?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Becoming easily annoyed or irritable?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Feeling nervous, anxious or on edge?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Not being able to stop or control worrying?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Trouble relaxing?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. Being so restless that it is hard to sit still?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

SECTION E: FOOT AND OTHER JOINT PROBLEMS

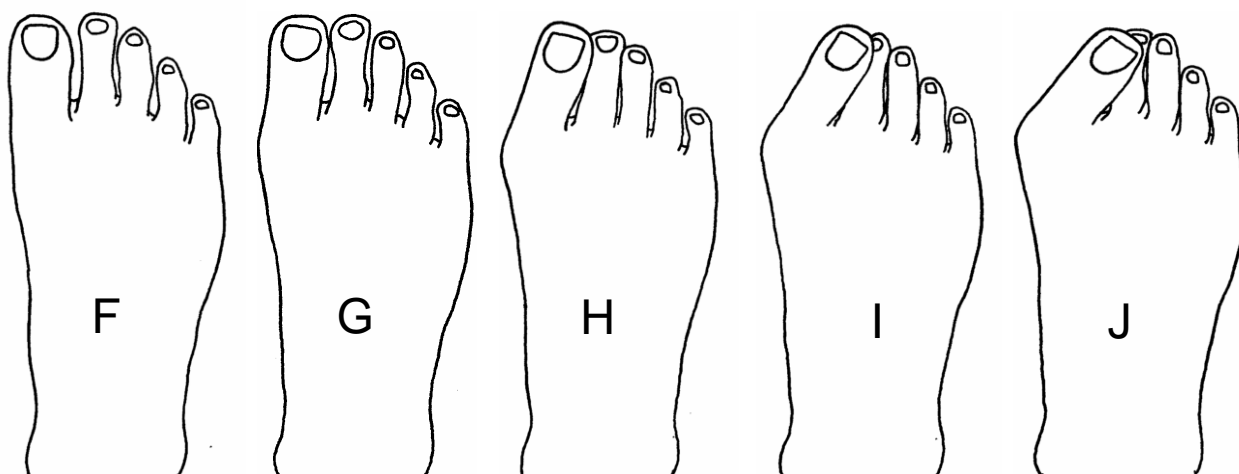
Part 1 - Feet

We are interested in whether your big toes are straight or angled sideways because this might be related to your ability to move around.

First, please look at your left big toe whilst standing **without shoes and socks on**. Ignore the positioning and the gaps between your other toes and try to focus **only** on your big toe. Select from the first set of pictures below labelled from A to E which one best shows the



Now do the same for your right big toe joint using the set of pictures below labelled from F to J. Again please **circle** the letter of the picture that best shows the angle of your right big toe.



Part 2: Pain and discomfort in the feet

1. In the **past month** have you had pain **or** aching **or** stiffness in your feet?

No days

☐

Few days

☐

Some days

☐

Most days

☐

All days

☐

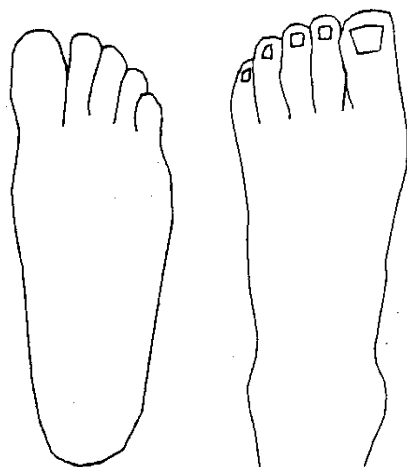
If 'No days' please continue with **question 4 on page 16**

2. This question is about any **recent pain** you have had in your **feet**. In the **past month**, have you had any ache or pain that has lasted for **one day or longer** in your feet? Please **do not** include pain due to feverish illness such as flu.

Yes..... ☐ → ***Please shade in the diagrams below any pain you have had in your feet in the last **month** that has lasted **one day or longer*****

No..... ☐

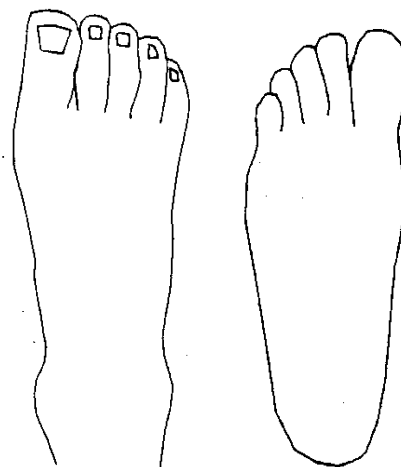
Left foot



Sole / bottom

Top

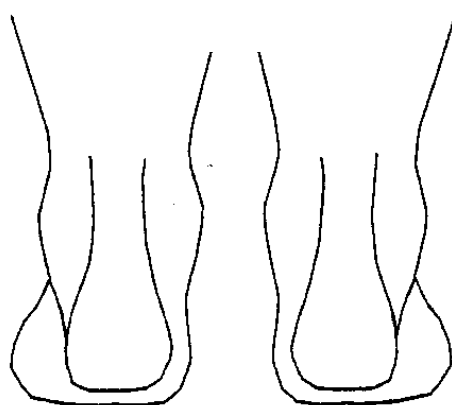
Right foot



Top

Sole / bottom

Ankles (back view)



Left

Right

3. Below are some statements about problems related to pain in the feet. For each statement indicate if this has applied to you **during the past month**.
(Please tick only one box for each statement).

	None of the time	On some days	On most / every day(s)
<i>Because of pain in my feet:</i>			
a. I avoid walking outside at all	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. I avoid walking long distances	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. I don't walk in a normal way	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. I walk slowly	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. I have to stop and rest my feet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. I avoid hard or rough surfaces when possible	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g. I avoid standing for a long time	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h. I catch the bus or use the car more often	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. I need help with housework/ shopping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j. I still do everything but with more pain or discomfort	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
k. I get irritable when my feet hurt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
l. I feel self conscious about my feet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
m. I get self conscious about the shoes I have to wear	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
n. I have constant pain in my feet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
o. My feet are worse in the morning	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
p. My feet are more painful in the evening	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
q. I get shooting pains in my feet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. Have you consulted your GP (family doctor) in the past 12 months because of problems with your foot or feet?

(Please put a cross in one box only)

Yes

☐

No

☐

5. Which of the following services have you used in the **past 12 months** because of problems with your foot or feet? For **each service** you have used please put a cross to show whether the NHS provided this, or if you had private treatment. If you have used both NHS **and** private services please cross both boxes. For any service you have not used please leave blank.

	NHS	Private
a. Physiotherapy	<input type="checkbox"/>	<input type="checkbox"/>
b. Podiatry	<input type="checkbox"/>	<input type="checkbox"/>
c. Chiropody	<input type="checkbox"/>	<input type="checkbox"/>

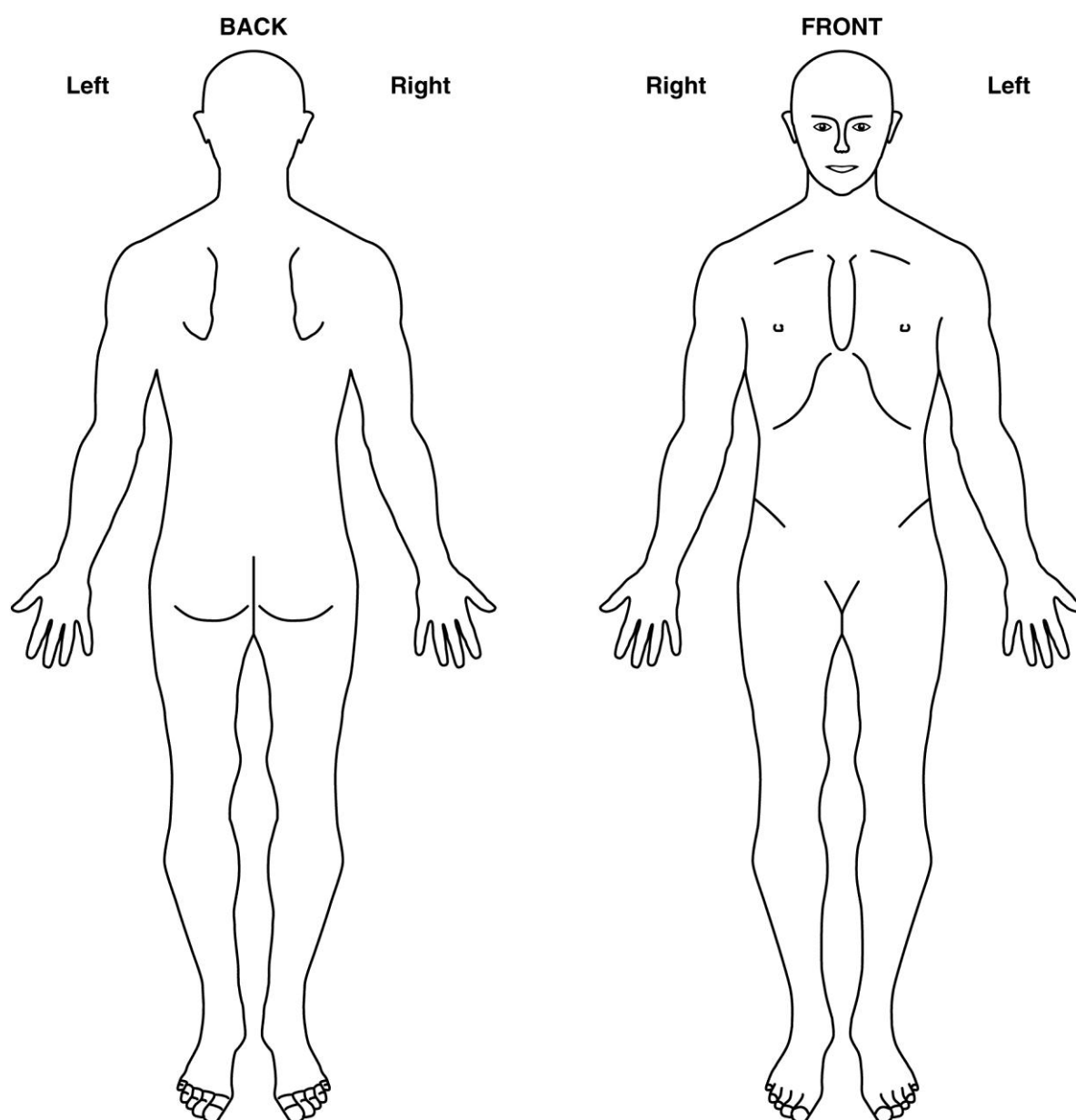
Part 3 – Body Chart

This question is about **recent pain** you may have had in **any part of your body**. By pain we also mean ache or discomfort or stiffness. Please **do not** include pain due to a feverish illness such as flu. If you are a woman please **do not** include pain related to your monthly period.

In the past 4 weeks, have you had pain that has lasted for one day or longer in any part of your body? (*Please put a cross in one box only*)

Yes..... ☐ → **Please shade in the diagram below any pain that has lasted for one day or longer in the past 4 weeks**

No..... ☐ → Please continue with **section F on page 18**



SECTION F: HOW GOUT AFFECTS YOUR WORK

THIS SECTION ASKS SOME GENERAL QUESTIONS ABOUT YOUR WORK

1. Which of the following best describes your **current** situation?

(Please put a cross in one box only)

- Working full-time in a paid job..... ☐
- Working part-time in a paid job..... ☐
- Employed, but currently off sick for 6 months or less..... ☐
- Looking after the home / children..... ☐
- Not working, for more than 6 months due to joint problems..... ☐
- Not working, for more than 6 months for other reasons..... ☐
- Fully retired..... ☐
- Early retirement due to joint / back problems..... ☐
- Early retirement for other reasons..... ☐
- Student..... ☐
- Other ☐

If 'other', please write in your current situation below:-

.....

2. Have you **taken time off work** during the last 6 months because of gout?

(Please put a cross in one box only)

Yes ☐ No ☐

3. Are you currently

(Please put a cross in one box only)

- a. Doing your usual job? ☐ *Please go to **Section G** on page 20.*
- b. Working fewer hours? ☐
- c. Doing lighter duties? ☐
- d. On paid sick leave? ☐
- e. On unpaid leave? ☐

If you have answered b) to e), please answer question 4.

4. If you are not doing your usual job, is this because of joint problems?

Yes ☐ No ☐

SECTION G: ABOUT YOURSELF

THIS SECTION ASKS SOME GENERAL QUESTIONS ABOUT YOU

1. What is your date of birth?

/

(E.g. – if you were born on the 5th of June 1936, this would be entered as 05/06/36)

2. Are you

Male ☐ Female ☐

3. What is your relationship status

(Please place a cross in one box only)

- | | | | |
|----------------------|--------------------------|------------------|--------------------------|
| a. Married..... | <input type="checkbox"/> | b. Widowed..... | <input type="checkbox"/> |
| c. Co- habiting..... | <input type="checkbox"/> | d. Divorced..... | <input type="checkbox"/> |
| e. Separated..... | <input type="checkbox"/> | f. Single..... | <input type="checkbox"/> |

4. Did you go on from school to full-time education or university?

Yes ☐ **If yes**, what age did you finish full-time education? years
No ☐

5. Is your ethnic origin? **(Please put a cross in one box only)**

- | | | | |
|---------------------------|--------------------------|-----------------|--------------------------|
| a. White UK/European..... | <input type="checkbox"/> | b. Asian..... | <input type="checkbox"/> |
| c. Afro Caribbean..... | <input type="checkbox"/> | d. African..... | <input type="checkbox"/> |
| e. Chinese..... | <input type="checkbox"/> | f. Other..... | <input type="checkbox"/> |

6. What is your height?

Feet inches OR cms

7. What is your weight?

Stones lbs OR kgs

8. About how often do you drink alcohol?

(Put a cross in one box only)

- a. Daily or almost daily..... ☐
- b. 3 to 4 times a week..... ☐
- c. Once or twice a week..... ☐
- d. 1 to 3 times a month..... ☐
- e. Special occasions only..... ☐
- f. Never..... ☐

9. In an **average week** how many

Number

- a. Small glasses (175 ml) of **wine** do you drink (there are roughly 6 glasses per bottle)?.....
- b. Pints of **beer** do you drink (includes bitter, lager, stout and ale)?..
- c. Measures of **spirits** do you drink (includes Whiskey)?.....

SECTION H: CONSENT FORM

Thank you for completing this questionnaire

The nature of the questionnaire is not meant to be distressing in any way. However, if the questionnaires lead to distress, unpleasant memories or thoughts, we would encourage you to contact your General Practitioner. You may also wish to contact an independent mental health support group, which does not require referral from a doctor or a nurse. All calls are free (call back also available), confidential and support is provided by trained staff. The phone numbers of these support groups are listed below.

Mental Health Helpline Staffordshire (Brighter Futures) 0808 800 2234

Mental Health Helpline Shropshire 0800 195 1700

Mental Health Helpline Wolverhampton 0800 387034

Please ensure that you have read the enclosed information sheet that explains about the study and other similar questionnaires that will be sent to you in 6, 12, 24 and 36 months time.

Please read, complete and sign the consent form on the following page.



Consent form

I confirm that I have read and understood the study information sheet and am willing to take part in the study. I understand that I can withdraw from the study at any time, and that this will not affect the care I receive in any way.

Please answer each statement by putting a cross in the box on each line

	Yes	No
I give my permission for my medical records to be reviewed by the research team as part of the study.....	<input type="checkbox"/>	<input type="checkbox"/>
I am happy to be contacted again (this does not mean that you must take part in future - you are just agreeing to be contacted again).....	<input type="checkbox"/>	<input type="checkbox"/>
I understand that my medical notes and data collected during the study may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to the records.....	<input type="checkbox"/>	<input type="checkbox"/>

Signed:

Date:

Title:..... Forename(s):.....

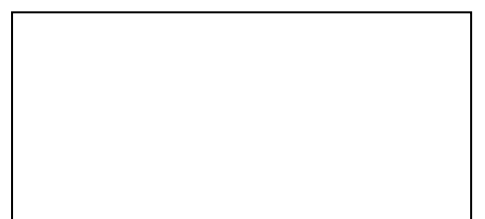
Surname:.....

Address:.....

Postcode:

Even if you would prefer us not to review your medical records or contact you again about the study, the answers you have given in this questionnaire will still be very important to us. Please return your questionnaire in the **FREEPOST (no stamp needed)** envelope provided. Thank you for your help with this research project.

For office use only:



Appendix 4: Data extraction of studies in the systematic review

	method of recruitment of participants	inclusion criteria	Exclusion criteria	Matched Controls	cases			Method of gout diagnosis	Response or attrition rate	Measure of association between gout and HRQOL	Follow-up duration	Cohort representativeness
					Age (years)	Sex	Ethnicity					
Singh, Strand 2008	VA database	veterans with gout	NR	64 553–69 410	68	99% male	97% white	ICD 9 codes	58%	Univariate and multivariate associations but no RR or OR presented	NA	Veterans only although comparable with some population estimates
Colwell, Hunt et al. 2006	Phase 2 clinical trial of febuxostat in gout patients	SUA >8 mg/dL	NR	NR	54	88.1% male	86.5% white	NR	82.4%	NR	12 months	No – clinical trial of febuxostat
Taylor, Colvine et al. 2008	20 patients with gout from a study of hand function in gout (recruited from OP clinic). Also	Wallace criteria	NR	NR	57 to 58	95% male (hand function group), 77% male (clinic patient	55% Maori 45% other (hand function group), 68% Maori	Wallace criteria	NR	NR	NA	No – from hand function study and secondary care clinic

	method of recruitment of participants	inclusion criteria	Exclusion criteria	Matched Controls	cases			Method of gout diagnosis	Response or attrition rate	Measure of association between gout and HRQOL	Follow-up duration	Cohort representativeness
					Age (years)	Sex	Ethnicity					
	53 consecutive patients from Rheumatology clinics					ts)	32% other (clinic patients)					
Hirsch, Terkeltaub et al. 2010	Clinics in 3 US cities (physician in house, patient response to clinic posters and newspaper advertisement). Physicians faxed details of diagnosis, tophi and SUA	Aged 18-85, gout as determined by a physician	NR	NR	62	90.2% male	75.9% White	ARA criteria	83%	attack frequency, pain during and between attacks associated with HRQOL	NA	Yes – patients from secondary and primary care
Hirsch, Lee et al. 2008	Participants identified from physician's	Aged 18-85, gout as determined	NR	NR	62	90.2% male	75.9% White	physician clinical diagnosis available	83%	Association between gout characteristics	NA	Yes – patients from secondary and primary care

	method of recruitment of participants	inclusion criteria	Exclusion criteria	Matched Controls	cases			Method of gout diagnosis	Response or attrition rate	Measure of association between gout and HRQOL	Follow-up duration	Cohort representativeness
					Age (years)	Sex	Ethnicity					
	clinics	identified by a physician						for 73.4% (SUA, crystal aspirate and radiographic findings)		tics and HRQOL		
Roddy, Zhang et al. 2007c	Questionnaire sent to all patients aged > 30 at 2 GP practices. Self-reported gout cases were clinically assessed and included or excluded as gout cases	>30 years, registered at one of the 2 GP practices	major psychiatric illness, dementia or recently diagnosed malignancy	2848	63.8	81% male	NR	clinical diagnosis-ARA criteria, tophi, SUA	23%	Physical HRQOL was significantly lower in cases than controls. No difference in HRQOL in gout cases based on SUA and allopurinol use. T test and Chi squared to test	NA	Yes – primary care based

	method of recruitment of participants	inclusion criteria	Exclusion criteria	Matched Controls	cases			Method of gout diagnosis	Response or attrition rate	Measure of association between gout and HRQOL	Follow-up duration	Cohort representativeness
					Age (years)	Sex	Ethnicity					
										difference between mean scores		
Dalbeth, Taylor et al. 2009	advertising in primary and secondary care clinics	Disease duration < 10 years	NR	NR	57	78% male	71% European, 29% Maori	Wallace criteria	93%	NR	1 year	Yes – primary and secondary care
(Alvarez-Hernandez, Zamudio-Lerma et al. 2009	NR	Tophaceous gout	NR	NR	53	100% male	NR	chronic tophaceous gout as defined by the ACR criteria	100%	NR	8 weeks	No – small sample size and only those with tophaceous gout
Lee, Hirsch et al. 2009	Adverts in primary and secondary care clinic waiting rooms	aged 18-85, self-reported or physician confirmed diagnosis of gout	NR	age matched US population without gout	62.2	90.2% male	75.9% Caucasian	Self-report (32%) and physician confirmed (68%)	83%	Yes	NA	Yes – primary and secondary care
Sarkin, Levack et al. 2010	Part of a larger study. In office	age 18-85, physician diagnosis	NR	NR	NR	NR	NR	ACR preliminary criteria	NR	Correlation between patient	NA	Yes- primary and secondary care

	method of recruitment of participants	inclusion criteria	Exclusion criteria	Matched Controls	cases			Method of gout diagnosis	Response or attrition rate	Measure of association between gout and HRQOL	Follow-up duration	Cohort representativeness
					Age (years)	Sex	Ethnicity					
	physician recruitment, patient response to clinic posters and newspaper adverts	of gout								and physician rated severity and HRQOL		
Becker, Schumacher et al. 2009	academic and private rheumatology clinics	18 years or over, had TFG (as defined by symptomatic crystal proven gout of at least 2 years duration and intolerance or refractoriness to conventional ULT	NR	NR	59	90% male	75% White	identification of MSU crystals on microscopy	47.3% completed follow up	Correlation between gout and co-morbid characteristics and HAQ-DI and SF-36	1 year	No -academic and private clinic setting, only those with TFG

	method of recruitment of participants	inclusion criteria	Exclusion criteria	Matched Controls	cases			Method of gout diagnosis	Response or attrition rate	Measure of association between gout and HRQOL	Follow-up duration	Cohort representativeness
					Age (years)	Sex	Ethnicity					
		with SUA>6mg/dl)										
Ten Klooster, Oude Voshaar et al. 2011	Secondary care rheumatology clinics	NR	NR	NR	58.9	82% male	NR	Urate crystals in 80% and elevated SUA in 20%	95%	NR	NA	No – recruitment in secondary care, small sample size (n=102)
(Khanna, Ahmed et al. 2008	Private clinic and University	aged 18 or over, ACR criteria for gout	acute gout flare in the last 4 weeks	NR	60	90% male	69% White	ACR criteria	NR	Health disutility scores with gout	NA	No – private clinics and not those with acute gout
Alvarez-Hernandez, Pelaez-Ballestas et al. 2008	8 rheumatology departments	NR	NR	NR	56.3	99.6% male	NR	ACR criteria	83.5% at 6 months	Correlation between HAQ-DI and gout, co-morbidities and SF-36	6 months	Yes
Khanna, Perez-Ruiz et al. 2011	Gout clinic	NR	gout flare in last weeks	NR	57.1	97% male	NR	MSU crystal proven	36.4% responded at end of FU	SF-36 correlation with gout characteristics	2 years	No - secondary care only, acute gout excluded

	method of recruitment of participants	inclusion criteria	Exclusion criteria	Matched Controls	cases			Method of gout diagnosis	Response or attrition rate	Measure of association between gout and HRQOL	Follow-up duration	Cohort representativeness
					Age (years)	Sex	Ethnicity					
Khanna, Sarkin et al. 2011	RCT of rilonacept versus placebo	>18 years of age with inter-critical gout, ≥ 2 flares in the past one year and not taking colchicine or steroid within 1 month of enrolment, SUA >7.5 mg/dl	Gout flare in 2 weeks preceding the study	NR	50.5	96% male	90.4% White	Self-reported	88% at end of follow-up	MCID in GIS reported for 7 patient reported anchors	8 weeks	No- RCT
Groen, Klooster et al. 2010	Outpatient rheumatology clinic	NR	NR	Unmatched controls with RA and OA	62	82% male	NR	Physician diagnosis	NR	NR	NA	No – secondary care clinic only
Alvarez-Nemegyei, Censante et al. 2005	Primary care medical units	Gout based on Wallace criteria	Subjects without MSK disability or renal	Unmatched controls	54	98% males	NR	Wallace criteria	NR	RR of disability, renal failure and gout	NA	Yes – primary care recruitment

	method of recruitment of participants	inclusion criteria	Exclusion criteria	Matched Controls	cases			Method of gout diagnosis	Response or attrition rate	Measure of association between gout and HRQOL	Follow-up duration	Cohort representativeness
					Age (years)	Sex	Ethnicity					
			failure							characteristics		
Singh, Sarkin et al. 2011	Part of a larger study. In office physician recruitment, patient response to clinic posters and newspaper adverts	Physician (ACR criteria) diagnosis or self-reported, aged 18 to 85 years, ability to provide physicians contact details	NR	NR	62.3	90.8% males	76% White	ACR criteria or self-reported	99.3%	Yes correlation and multivariate regression analysis (logistic)	NA	Yes- primary and secondary care
Khanna, Nuki et al. 2012	Recruited from the NHWS and LSR ailment panel	NR	NR	NR	60.9	81% males	NR	Self-reported	39%	Multivariate regression models giving rate ratios	NA	Yes- recruited from USA and EU general health surveys

Abbreviations: NR- not reported, NA- not applicable, MSU- monosodium urate, SUA – serum uric acid, TFG –treatment failure gout, ICD – international classification of diseases, ARA- american rheumatology association, ACR – american college of rheumatology, MCID- minimal clinically important difference, HRQOL –health related quality of life, RR – relative risk, OR –odds ratio, NHWS – national health and wellbeing survey, LSR – lightspeed research, MSK –musculoskeletal, GIS – gout impact scale, HAQ-DI –health assessment questionnaire disability index, SF-36- short form-36.

**Appendix 5: The Gout Study_covering letter sent with baseline
questionnaire booklet version 1.0 dated 15 02 12**

GP Practice Name
GP Practice Address
GP Practice Telephone Numbers

Patient's Name

Patient's Address

Patient's Postcode

Date

Study ID

Dear (insert name),

The doctors in this practice are working with researchers in the Arthritis Research UK Primary Care Centre, at Keele University. We are writing to you to see if you would be willing to help us with a research project.

Researchers at Keele University are trying to find out about **gout**, to get a better understanding of this condition. Further details of the project are on the accompanying Participant Information Sheet.

You have been sent this letter because you have been to see your GP with gout or have taken medications for gout during the last two years. We hope that you will be able to spare a short amount of time to complete the enclosed questionnaire. It should take you no more than 30 minutes to fill in.

All of your answers will be dealt with in strict confidence. We can also assure you that whether or not you answer the questionnaire will not in any way affect the care you receive from this practice or elsewhere.

We would be very grateful if you would return the questionnaire in the envelope provided in the next two weeks. **You do not need a stamp.** A short while after this date, we will send a reminder to people whose questionnaire we have not received. If you would like to know more about this study, please contact **Priyanka Chandratre**, at Keele University on **01782 734721**.

We will be asking you if you would be willing to help with this research study in the future, so we will also ask your permission to contact you again at the end of the questionnaire. In addition, we will ask your permission for review of your medical records. Full details of this research study are provided in the enclosed Participant Information Sheet.

Thank you very much for your help with this research project.

Yours sincerely,

Name of GP(s)

Enc: Participant information sheet, gout questionnaire, pre-paid envelope

The Gout Study – covering letter sent with baseline questionnaire booklet, version 1.0, dated 15/02/12

**Appendix 6: The Gout Study_Participant Information Sheet for Gout Study
version 2.0 dated 08 05 12**

PRIMARY CARE SCIENCES
ARTHRITIS RESEARCH UK PRIMARY CARE CENTRE

PATIENT INFORMATION SHEET
REC Reference Number 12/NW/0297
Version 2.0, dated 08/05/12

The Gout Study

You are being invited to take part in a research study. Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

What is the purpose of the study?

Your GP practice, together with Keele University, is carrying out a research study on gout. Gout is the most common cause of inflamed joints in adults and can recur from time to time. Despite this, little is known about the way gout can affect peoples' quality of life and how to identify and treat those who may be at risk of having a worse outcome than others. We are trying to find out more about how gout affects people in the community and how it changes over the time.

Why have I been invited?

You were selected because you have been to see your GP with gout or you have taken medication for gout during the last two years.

Do I have to take part?

Whether or not you take part in this research is up to you. If you do decide to take part, you are free to withdraw at any time without giving a reason. A decision to withdraw, or a decision not to take part, will not affect your right to access health services at your practice or elsewhere.

How long will it take?

Taking part in this study means that you are asked to complete the enclosed questionnaire. We will also send you another similar questionnaire in 6, 12, 24 and 36 months' time. We think it should take up to 30 minutes to complete each questionnaire.

Future contact

In the future, we may contact you again to ask you further questions about gout. We ask for your permission to contact you again on the last page of the questionnaire. If you agree to be contacted again, this does not mean that you must take part in future; you are only agreeing to be contacted again.

What are the possible benefits of taking part?

Although there are no immediate benefits to you as a patient, we hope that the insight we gain from this research will help patients in the future. Your participation will help us to learn more about gout and how to best treat it in general practice.

What are the possible risks of taking part?

The nature of the questionnaire is not meant to be distressing in any way. However if the questionnaires lead to distress, unpleasant memories or thoughts, we would encourage you to contact your General Practitioner. You may also wish to contact an independent mental health support group, which does not require referral from a doctor or a nurse. All calls are free (call back also available), confidential and support is provided by trained staff. The phone numbers of these support groups will also be provided at the end of each questionnaire.

Mental Health Helpline Staffordshire (Brighter Futures) 0808 800 2234

Mental Health Helpline Shropshire 0800 195 1700

Mental Health Helpline Wolverhampton 0800 387034

Will my taking part in this study be kept confidential?

The answers you give in the questionnaire will be dealt with in **strictest confidence**. Each person who responds to the questionnaire will be given a code number, so the data from the study will not have any identifiable names and addresses, and cannot be traced back to you. On this basis, the data may be used in other research studies.

How long will the answers to the study questionnaires be stored for?

The questionnaires will be stored without identifiable names and addresses for twenty years in accordance with the Medical Research Council guidelines. Beyond this date records will be maintained if the study is still on-going. The questionnaires will be stored in a secure place. Any identifiable personal information such as your name and address will however be destroyed at the end of the study period. This will ensure that personal data will not be stored for longer than is necessary (Data Protection Act 1998).

Medical record review

Another part of this study is to find out what other factors related to gout, such as your medications and other health problems may influence your quality of life. We can do this by reviewing your medical records, and we ask your permission to do this on the last page of the questionnaire. When reviewing medical records, your name will not be used so that you cannot be identified personally. All information will be held in strictest confidence.

What will happen if I don't want to carry on with this study?

You can withdraw from this study at any stage by contacting **Priyanka Chandratre**, the Gout Study Co-ordinator on **01782 734721**. Withdrawing means that we would no longer contact you directly, but we would still keep and use the information you have provided up to the point of your withdrawal. If you contact us to withdraw from the study, and you have consented to medical record review, we will check whether you also want us to stop reviewing your medical records.

What will happen to the results of the research study?

Because this is a large study, the results will not be available for about three years, and will then be published in medical journals and reports. The main findings from the study will be displayed on a poster in your practice. If you would like any other information after seeing this poster we will be happy to help.

Who is funding and organising the research?

The research is funded and organised by the Arthritis Research UK Primary Care Centre at Keele University.

Who has reviewed the study?

The Liverpool East Research Ethics Committee has reviewed this study (Research Ethics Committee Reference Number: 12/NW/0297).

Contact for further information

If you have any questions, or would like further information, about this study please contact **Priyanka Chandratre**, the Gout Study Co-ordinator on **01782 734721**. If you have any questions or concerns about taking part in this research you can also contact the Patient Advice and Liaison Service (PALS). Your local PALS office phone number for NHS Stoke-on-Trent is 0800 783 2865, Wolverhampton PCT is 01902 445378, NHS Telford and Wrekin is 01952 580478, NHS Shropshire county is 01952 580474, NHS South Staffordshire is 01543 465106 and for NHS North Staffordshire is 0800 030 4563.

Thank you for taking time to read this information leaflet.

Appendix 7: The Gout Study_invitation letter sent regarding the focus group interview version 1.0 dated 15 02 12

PRIMARY CARE SCIENCES
ARTHRITIS RESEARCH UK PRIMARY CARE CENTRE

Name

Address

Date

Study ID

Dear (insert name),

The Gout Study Interview

Thank you for your recent response to our questionnaire about gout, in which you kindly agreed that we could contact you further. We hope that you will be interested in taking part in the interview stage of this study. Before you decide please take time to read the enclosed information sheet. This tells you why the interview is being carried out and what is involved if you agree to take part.

Once you have decided whether or not you are interested in the study please return the enclosed reply slip in the stamped addressed envelope provided. **Whether or not you take part in the interview will not affect your current or future health care in any way.** If you have any queries about the interview, please do not hesitate to contact **Priyanka Chandratte**, the Gout Study Co-ordinator on **01782 734721**.

Thank you for taking the time to read the letter and the information enclosed.

Yours sincerely

Dr Edward Roddy
Clinical Senior Lecturer in Rheumatology and Consultant Rheumatologist

Enc:

The Gout Study Participant Information Sheet for gout interview (version 1.0, dated 15 02 12)
The Gout Study Focus Group Interview - Reply form

The Gout Study Focus Group Interview Reply Form

Please tick one box and return this form in the stamped addressed envelope provided. Thank you very much for your time and co-operation.

☐ Yes **I would like to take** part in the interview part of the gout study.

☐ No **I do not wish to take part in** the interview part of the study.

Name _____

Telephone _____

Address _____

Email _____

Please return the form in the envelope provided. **You do not need a stamp.**

**Appendix 8: The Gout Study_two week reminder letter for focus group
interviews version 1.0 dated 15 02 12**

PRIMARY CARE SCIENCES
ARTHRITIS RESEARCH UK PRIMARY CARE CENTRE

Name
Address
Date

Study ID

Dear (insert name),

The Gout Study focus group interview

Reminder invitation to take part in the interview

I write to remind you of the invitation to take part in the interview stage of the gout study. I appreciate that you may have been busy. If you have already contacted the Centre in the last few days I apologise for troubling you again and please ignore this letter.

We are contacting you because you recently completed a questionnaire about gout. We would like to talk to you about what it is like to have gout and what you would like your gout treatment to achieve or improve. The overall aim is to find out what aspects of gout and its treatment matter most to you.

I have enclosed another copy of the information sheet explaining the study in more detail and how you can take part. Whether or not you take part in the interview will not affect your care now or in the future. Once you have decided whether or not you are interested in the study please return the enclosed reply slip in the stamped addressed envelope provided. If you have any queries about the interview, please do not hesitate to contact **Priyanka Chandratre**, the Gout Study Co-ordinator on **01782 734721**.

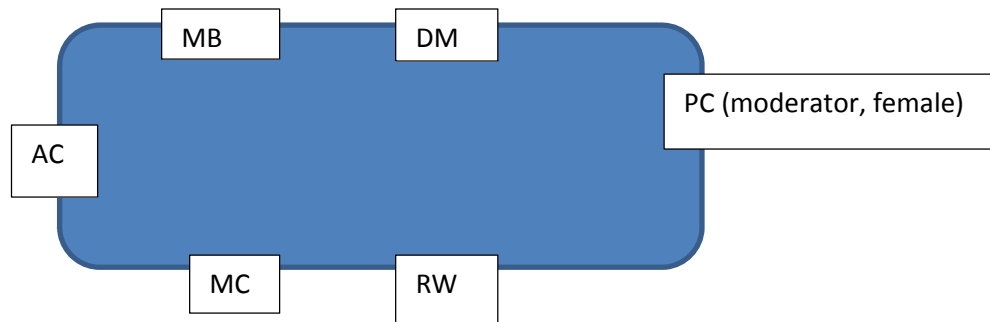
Yours sincerely,

Dr Edward Roddy
Clinical Lecturer and Honorary Consultant Rheumatologist

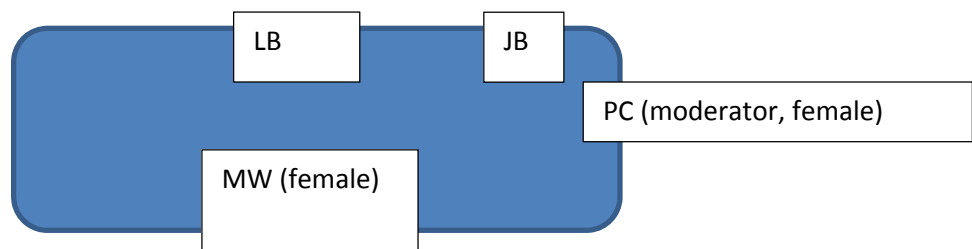
Enc: The gout study Participant Information Sheet for gout interview version 1.0 dated 15 02 12, Reply form

Appendix 9: Seating plans for focus group interviews

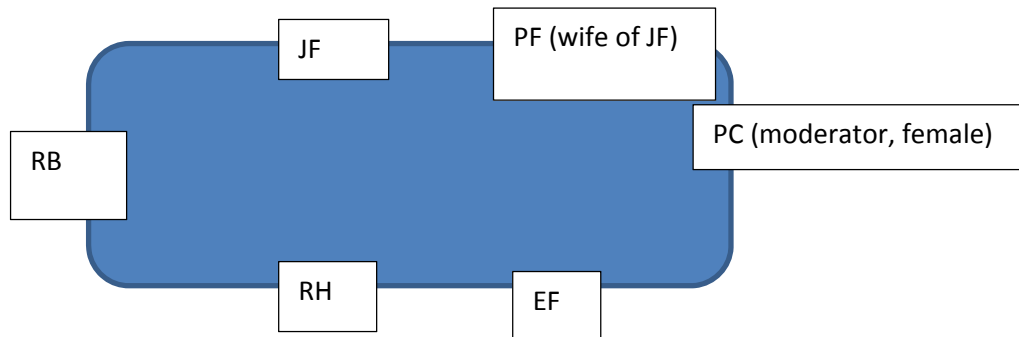
Gout focus group 1 03 12 12 recorder 1



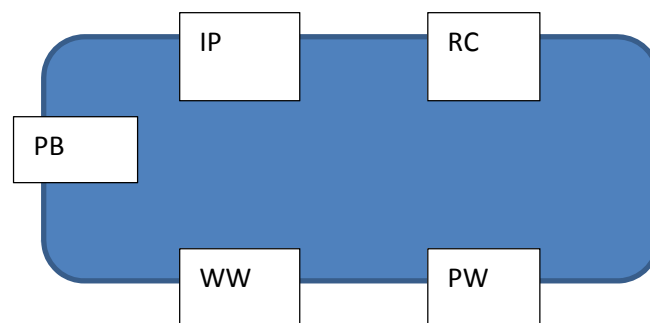
Gout focus group 2 06 12 12 recorder 1



Gout focus group 3 07 12 12 recorder 1



Gout focus group 4 13 12 12 recorder 1 (first and second part)



**Appendix 10: The Gout Study_Participant Information Sheet for Gout
Interview version 2.0 dated 08 05 12**

PRIMARY CARE SCIENCES
ARTHRITIS RESEARCH UK PRIMARY CARE CENTRE

PATIENT INFORMATION SHEET
REC Reference Number 12/NW/0297
Version 2.0, dated 08/05/12

Your views about gout and its impact on your life
– The Gout Study Focus Group Interview

We are contacting you because you recently completed a questionnaire about gout. You are now being invited to take part in a research interview about gout being conducted by the Arthritis Research UK Primary Care Centre, Keele University. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve.

This leaflet explains what will happen if you agree to take part in the study. **Please take time to read the following information carefully and discuss it with others if you wish.** If there is anything that is not clear or if you would like more information then please contact Priyanka Chandratre, the gout study co-ordinator on 01782 734721.

Thank you for taking the time to read the information below.

What is the purpose of the Interview?

Previous research has shown that gout can affect people's quality of life in several ways. We would like to talk to you about what it is like to have gout and what you would like your gout treatment to achieve or improve. The overall aim is to find out what aspects of gout and its treatment matter most to you. We hope that the research will help us to understand better what having gout means to patients so that we can improve the way gout is managed in general practice.

Where will the interview take place?

The interview will take place either at the Arthritis Research UK Primary Care Centre, Keele University or at your GP surgery.

Do I have to take part?

You have been chosen because you agreed to further contact from the study team here at the Arthritis Research UK Primary Care Centre when you filled in a questionnaire earlier this year. This questionnaire was called “**The Gout Study**”.

The next stage of the research involves interviewing people who have gout and we would like to invite you to take part in this. You are, of course, entirely free to decide whether or not to take part. If you do decide to take part you will be asked to sign a consent form at the time of the interview. If you decide to take part you are still free to withdraw at any time, and without giving a reason. Your decision as to whether or not to take part in the study, or any decision to withdraw from the study, will not affect the treatment you will receive, or any of your legal rights.

What will happen to me if I take part?

You will take part in a focus group interview. A group of people, all with gout, will take part in a discussion. We will talk about what it is like to have gout, your views about the treatments you may have had for gout and what you would like the treatment to achieve or improve. The focus group interview is likely to last about one and a half hours. There will be approximately 5 people in the group. We are interested in your views and experiences. There are no right or wrong answers. No preparation for the interview is necessary.

We would like to tape-record the interview and will check that is convenient with you at the time. The interview will then be typed out. Quotations from the interview may be used in reports of this study. Your identity will be hidden in any such report, and you will not be identified personally. The fact that you have taken part in the study will not be revealed to anyone outside the research team. If the interview contains comments or information that might identify a third party, or an institution (e.g., a GP, clinic or hospital), we will ensure that the person or institution cannot be identified in any account or published report of this study. You will be asked at the end of the interview if you are still happy to be included in the study. If you decide that you are no longer happy to do so, the information gathered in the interview will not be used and we will not contact you again.

How long will information gathered from the interview be stored for?

Both the tape (in a digital format) and the paper copy of the interview will be stored in a secure location for 20 years in keeping with guidance issued by the Medical Research Council and after this time they will be destroyed. Neither the audio tape nor the paper copy will bear any information that would identify you by name. Both the tape and the paper copy of the interview will only be accessed by a small team of researchers working at the Arthritis

Research UK Primary Care Centre. Any identifiable personal information such as your name and address will be destroyed at the end of the study period. This will ensure that personal data will not be stored for longer than is necessary (Data Protection Act 1998).

What are the possible benefits or risks of taking part?

There are no risks relating to medical treatment in this study. Neither is there intended to be any medical benefit. There may be an indirect benefit to you and other patients from the insights we gain from this study, but we cannot be sure about this. If an interview topic brings back unhappy memories or distressing thoughts that you do not wish to discuss, the topic will not be followed up again during the interview. During the interview, you can choose not to answer questions, or to end the interview at any time, and for any reason. You will also be offered the option of leaving the place where the interview is being held should you wish to do so.

What will happen to the results of the interview?

Because this interview is part of a large study, the results will not be available for about three years, and will then be published in medical journals and reports. The main findings from the study will be displayed on a poster in your practice. If you would like any other information after seeing this poster we will be happy to help.

Who is organising and funding the research?

This study is part of a programme of work into gout being conducted and funded by the Arthritis Research UK Primary Care Centre, at Keele University.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, well-being and dignity. This study has been reviewed and given a favourable opinion by the Liverpool East Research Ethics Committee (reference number 12/NW/0297).

How can further information about the study be obtained?

We will be glad to answer any questions that you may have about this study. For further information please contact Priyanka Chandratre, the gout study co-ordinator at the Arthritis Research UK Primary Care Centre, at Keele University on 01782 734721.

Thank you for taking the time to read this leaflet.

Appendix 11: Thematic analysis 4 stage conceptual overview

Higher order theme	Sub-theme	Text	Codes	Transcript number	Line
Gout characteristics	Pain	so I can't really go anywhere or do anything in that sense	Isolation and disability related to attacks	3	229-230
		You're so bored sat there not being able to move your foot, [laughter] that you get psychological side effects.	Inability to move causes boredom	1	632
		I'll get into freezing cold water and sit there. [yeah] I take that pain to take that off	Desperate measures to relieve the pain	3	739
		You can't turn over, when you're half asleep, you accidently touch something. You're frightened that she's going to touch it	Pain aggravated by contact	1	533
		But mine lies all over my body, everywhere. From one to another. [right] All down one side, well everywhere	Location of pain	3	14-15
		the bad attack will last maybe two or three weeks afterwards	Duration of attack	3	227
		But I always had a low level of pain for the last eight years I suppose	Long-standing pain	1	56
		you really bang your head against the wall	Severe pain	3	412
		It gets that painful I'll cry. I can't get rid of it.	Crying due to pain	3	737
	Unpredictable nature of attacks	the only reason that erm I went back this time to - to see about it was the fact that I was a little bit frightened if I was going to go on holiday the next day it was going to clobber me that day	Fear of uncertain nature of attacks	3	248-251
		It's the unpredictability of it, you know, you make a plan to, I don't know, maybe go to theatre in five weeks' time and when it gets closer you think god, I hope I don't get gout just the night before	Fear of breaking commitments due to unpredictable nature of attacks	3	401-403
	Gout more painful and harder to treat than	If it breaks, [yeah] you go to the hospital, put it in plaster, and you're - a bit of a throbbing and it's gone,	Fractured limb less painful and	3	754-756

Higher order theme	Sub-theme	Text	Codes	Transcript number	Line
Understanding of gout	other conditions	but with gout it's bang, bang, bang for days and days	has effective treatment		
	Severity dependent on joint involved	I mean a toe is relatively innocuous, if you've got it in your knees or hips or something, then yeah, it's a little more worrying	Concern for gout based on joint affected	2	232-233
	Lifestyle modification	Well I couldn't get my shoe on, last - a week ago since my last one	Difficulty with ADLs	3	111-112
		Because the damp weather, the cold and damp weather, is just not helping him at all. And they moved, they sold up and they moved to warmer climates	House move to avoid the cold which worsens symptoms	3	307-309
		I stopped doing these high impact erm exercises, I stopped long distance walking, because it was painful	Unable to exercise	1	59
		Like it's office work now, like you know a desk job now	Change in work environment	3	475
		Well we can't go out and do the same things	Change in social life since diagnosis	3	1402
		I could go out and leave him. [right, yeah] But there's no way I would. [okay] So it does have an effect on the whole unit	Family members restricted as well	3	1403-1404
		I'm a long distance runner, so when I can't run like I hate it..	physical disability	3	343
	Over-indulgence	Yeah I know I kind of guess when I might be getting one, [yeah] by the fact that I've over indulged somewhere	Pre-empting attacks when eaten or drank too much alcohol	3	63-64
	Gout not a disease but natural	For me, disease is something like malaria and erm... But it isn't is it, it's just a build-up of stuff that's naturally in your body	Gout as a natural illness rather than infectious	1	1062-1066

Higher order theme	Sub-theme	Text	Codes	Transcript number	Line
	Denial about gout	But the shock was saying I've got gout.	Gout as a shocking diagnosis	3	114
		I suppose I was a bit in self-denial, I don't suffer from gout	Self-denial	1	70
		there's more people than what we think who get it a bit, not coming forward and saying this is a bigger serious problem	Common and serious	3	420-423
		In fact I would put it down to aches and pains getting aged really rather than anything	Symptoms attributed to ageing	2	68-69
		You don't brag about it do you?	Gout not talked about openly	1	681
		Straightaway it's with the well-off people and [that's right, yeah] and the rich food.	Rich people and food associated with gout	3	114-115
		it's this thing erm...they don't realise what it is and they just use the old wives' tale, the port and pheasant, rich living	Ignorance and stereotypical views towards causes of gout	3	427-429
		No, you go in, you go in, you're the doctor, how much do you drink? I said I don't drink doctor			
	Gout not taken seriously	I think there's certain diseases that are quite humorous to - and they're not, but they're humorous to everybody else who hasn't got them	Gout treated with humour by those unaffected by it	2	439-441
		It happens so quick, people just don't believe it.	Sudden onset means people do not believe the intensity of symptoms	4	1078-1079
	Gout understood only by close contacts	when you've got gout your partner or friend or whatever, if they see you with gout when it's bad, they	Only close contacts will	3	957-959

Higher order theme	Sub-theme	Text	Codes	Transcript number	Line
		suddenly realise how bad it is	realise the true nature of gout		
	Lack of information from HCP	I found out for myself basically. [okay] So the doctor didn't really explain it that well	Self-researched information	1	256
		We've all got ignorance of it. Doctors don't sort of explain exactly what it is	Lack of knowledge of gout in patients and HCP	4	128-129
		I'd like to know the side effects though, properly [yeah] from a doctor, and not from the internet	Lack of information about side effects from HCP	3	257-258
	Lack of knowledge about dietary causes and treatments	Oh they put everything on there. What am I going to eat? You have to take it with a pinch of salt.	Many dietary restrictions	3	273-275
		When I looked onto NHS Direct, after I'd got it, that frightens the life out of you if you do anything because you get five pages	Overwhelming information	1	15
		it's just a great muddle about when it comes to food	Unclear about dietary causes	1	890
		Give them a 12 month diary or something like that. [right] And write each day what they've done that day. [okay] What they've drunk that day. What they've eaten that day. [yeah] And do a research programme like that and maybe you could come up with some facts	Research warranted on dietary intake and gout	3	1072-1074
	Need for better education about the symptoms of gout	my experience would be it should be publicised more that you know these sort of aches and pains [right] that you think you're getting as you go into old age	Better education about differentiating gout from old age	1	1511-1513
	Gout not as important	I don't think it's perceived to be life threatening,	Gout not life-	4	1144-

Higher order theme	Sub-theme	Text	Codes	Transcript number	Line
Treatment	as other conditions	whereas cancer and heart attacks are	threatening		1145
		They should spend more money on stuff which we ain't brought this on ourselves, [yeah] it's because it's an illness, it's - whatever it is, we've got with us, whereas drugs and - they'll spend money	More funding for gout than 'self-induced' conditions such as drug abuse	3	1364-1367
	Self-management	No I just treat myself now	Self-treatment	3	158
		when I found out it was gout I changed my lifestyle and stopped drinking	Change in lifestyle		
		I have cherries. And I have seeds sometimes, celery seeds	Cherry as treatment	3	605
		I find it quite manageable with erm anti-inflammatory tablets I take for it, [okay] along with the gastric tablet for the tummy	NSAIDs ⁴⁴ as treatment	3	28-29
		From the whatsit, the chemist'	Treatment from chemist	3	168
	Lack of contact with HCP	have a supply if I can feel it coming on, because I've got a spare box at home	Self-treatment with left over medications	3	197-198
		I dropped it down myself to one a day, I don't know what the doctor will say when I tell him	Allopurinol reduction without medical advice	1	464
		So it takes three, like it can take five days to see my doctor. You know, so by the time I get in there it'll probably have eased down a lot	Delayed presentation due to lack of GP appointment	3	485-487
	Reluctance to prescribe and take allopurinol	he could prescribe one to have one every day like for the rest of my life he says I wouldn't really recommend	Physician recommended	3	185-187

Higher order theme	Sub-theme	Text	Codes	Transcript number	Line
		it if you can get away with it, just come in if you start getting an attack	treatment of acute attacks only		
		He's sick of tablets like me	Fed up of taking medications	3	202
		he asked me would you like to take a tablet every day of your life and I says not really, no, like you know I really wouldn't want to be on that sort of thing, I said I'd rather stick to it where I can have a tablet and get it	Patient reluctance to take lifelong ULT	3	194-196
		I find mine just goes quickly, so I'm tremendously happy, I wouldn't want to be on long term Allopurinol, not because there's anything wrong with it, or anything, or anything else, I'm very, very content with what I've got	No concerns regarding allopurinol but prefers treatment of acute attacks only	2	342-345
		and then you go - and then you get gout, it gives you gout	Allopurinol induced gout attack	1	299-300
		I said I'm not being funny here but can I have this one please because this one seems to be the new one, and much better. She didn't offer it because it's obviously more expensive	New medication superior to existing, HCP reluctant to prescribe due to cost	1	156
		I'm old enough now that another tablet for the rest of my life doesn't make a lot of difference	Age a deciding factor in accepting ULT	3	252-253
	Concerns about side effects of treatment	My kidney function, he always checks because I think it's on the border line, so I think that might have been one of the reasons he was a little bit wary about erm prescribing Allopurinol	Difficult to treat gout in the presence of renal disease	1	1007

Higher order theme	Sub-theme	Text	Codes	Transcript number	Line
		Because of the other medication that he takes, the gout tablets don't sit well	Interaction with other medications	3	545-546
		My medic said that Allopurinol can actually cause gout to flare up again. If I had any problems, any pain, [yeah] to stop taking it immediately.	Allopurinol should be stopped during an acute attack	1	172, 177
	Benefits of treatment	you go two for I think it's two months, I've forgotten now, [yes] and then you go to three, and then that is - that's a miracle	Increase in allopurinol dose stops acute attacks	1	298-302
		Go to the doctors and get the pills... I wish he'd done it two years ago	Recommend immediate treatment with ULT	1	577, 1280
		Well I'm still eating mussels and king prawns and everything like that. The Allopurinol I suppose is to let you do that isn't it?	Maintaining usual lifestyle if on ULT	1	1349-1350

Abbreviations: NSAIDs – non steroidal anti-inflammatory, ADL – activities of daily living, ULT – urate lowering treatment, HCP –healthcare provider, CVD – cardiovascular diseases

Appendix 12: Focus group interview transcripts

1 **Focus group interview transcript 1**

2 PC: = MODERATOR

3 M: = MALE PARTICIPANT

4 F: = FEMALE PARTICIPANT

5

6 M: Yeah.

7 M: Didn't know it.

8 M: Didn't know it. You had other pains and...

9 M: Other pains, and I'd been on medication for six weeks [oh right], and it's changed.

10 M: Yeah, six weeks? [yeah] What, the gout medication? [yeah] Right. How long have you
11 been on it?

12 M: Well I haven't got it at the moment, erm...it's a couple of years ago and I sort of started
13 looking at sort of healthier eating regime, [yeah] erm little did I realise that - I made a
14 list of the things that I started eating, and when I looked onto NHS Direct, after I'd got it,
15 that frightens the life out of you if you do anything because you get five pages, very,
16 very good, like what is it, how do you get it, what causes it, what can you do about it,
17 how do you treat it, and it was a fantastic thing, so after I'd first got it, sorry, are we just
18 kicking off?

19 PC: Yeah, well okay so let's start. Yeah.

20 M: It was really interesting and when I looked onto the NHS Direct site erm how do you get
21 it, what's - and the uric acid thing, so we all know that I guess [yeah], but what you don't
22 know is what foods have uric acid in them. And it's just amazing what...

23 M: Because isn't it part of a protein?

24 M: It's yeast, it's something to do with yeast.

25 PC: Yeah, so there's a type of protein called purin and foods that are rich in that, that tends
26 to bring on gout attacks. Erm and there isn't - there's a sort of school of thought that it's,
27 you know, if you drink too much, certain types of alcohol particularly beer and spirits
28 rather than wine or if you have a high consumption of red meat which contains purin or
29 sea food, shellfish, that sort of thing, erm...

30 M: See that's classic, yeah.

31 PC: So erm, yeah.

32 M: There is one interesting point on the NHS site, and it says that if you injure a joint that
33 can [yeah] cause gout to come on and I'd like to discuss that with you.

34 PC: Yes, erm...yeah, no, we'll come to that if that's okay, Alan. Erm what we'll start off with,
35 if you don't mind, is just I wanted to find out really about what your views are about
36 how gout has affected you, and you know please your personal experiences by all
37 means, how that has affected your life in general, and different aspects of your life. and
38 try and focus on the treatment, so what I want to know is how did you start on
39 treatment, are you satisfied with it, what do you think of it, what do you want it to
40 improve or achieve, if you're not satisfied with it, do you understand why you're on it,
41 that sort of thing, you know. So that's sort of erm - and then we'll come back to your...

42 M: Well that relates to my question about [okay] when - when are you suffering with gout?
43 If I give you my experience, [yeah] up until 10 years ago I was very active, erm I was one
44 of these fitness fanatics. And I used to have - always have problems with my left foot,
45 erm and I originally put it down to the fact that I'd injured it playing squash, running,
46 long distance walking, all these sorts of things, and I used to have what I used to think
47 was a sprained foot with a lot of pain. Erm I also had a problem with my little toe, and
48 they ultimately, about six years ago, removed it. But I always had a low level of pain for
49 the last eight years I suppose, erm and when I walked I would get sharp pains, very
50 sharp pains, it was very uncomfortable, so I changed my lifestyle. I - I stopped doing
51 these high impact erm exercises, I stopped long distance walking, because it was painful.
52 [okay] Then over perhaps the last four years, erm I started having probably about every
53 six months a sudden real bad attack of pain in my left foot, which I used to be able to
54 link to doing stupid things like shifting three tons of gravel in a morning and sprain, and I
55 used to think I'd sprained my foot. And erm it would swell up, I would have
56 physiotherapy on it. I suppose in some respects, and this is why I ask whether you had
57 access to our medical records, I think I was told I had a fairly high uric acid [yeah]
58 content in the blood, but it wasn't, if you like, directly diagnosed as being gout.

59 PC: As gout, yeah.

60 M: And erm I suppose I was a bit in self denial, I don't suffer from gout, [yeah]. Erm but
61 then I started having - I didn't have the classic symptoms, I'd have a swelling of the foot,
62 but it wouldn't be red, it wouldn't be erm something that you couldn't touch, but
63 searing pains in the foot, as though somebody was putting a red-hot poker up through
64 the base of the foot.

65 PC: That's interesting, I mean what - so what sort of made you go into self denial, what is it
66 about gout that you didn't want to accept? [laughter]

67 M: It's an old man's, real old man's...

68 M: It's an old man's erm...yeah.

69 M: It was a rich man's yeah...

70 M: Yeah, yeah. You know, it's someone with...

71 M: Too much rich food.

72 M: ...and unhealthy lifestyle.

73 M: Port and stilton cheese diet.

74 M: I think a fair...yeah.

75 M: I can vouch for the port thing. [yeah]

76 PC: Right, yeah. And - and you - so typically, because you said it's not, you know, throbbing,
77 people can't touch it, is that how you see gout? Is that your state?

78 M: Well that's - everybody that I've spoken to about gout has said, you know, they couldn't
79 even bear the weight of bedclothes on their foot.

80 M: A sheet in the summertime.

81 M: Whereas I could...

82 M: Even a single sheet in the summer was absolutely - I had to have my foot [yeah] sticking
83 out of the bed.

84 M: Foot out, sticking out of the bed.

85 M: And it was summertime, so we didn't have any blankets, just a sheet, it was quite warm.
86 Just the sheet...[okay]

87 M: Well we went, we went to...France about five years ago, and erm I was due for
88 retirement sort of thing like, well longer, about eight years ago, and erm we bought a
89 fromage frais fruits of the forest cake from erm - I forget the place now, but we bought
90 this cake and we went back - went back to erm home, and erm about 1 o'clock in the
91 morning we cut this cake in half, into quarters, and had a quarter each. I never worked
92 again. [laughs] I had gout in my chin, [chin?] yeah, [what?] yeah, [strange] I had - all my
93 [6:34] swelled up, erm my elbow swelled up, [yeah] both knees, both ankles, both big
94 toes, [right] I could hardly walk.

95 PC: Right, right. Okay.

96 M: That's interesting about you saying having gout in the chin, [yeah]. One of the things
97 that I...

98 M: I broke my chin by the way.

99 M: ...one of the things that I've noticed since I've been on this medication, I still do
100 stretching exercise because I play golf, [okay] and I always have licking in my joints, this
101 Allopurinol for six weeks, it's gone.

102 PC: So you're better with the tablets?

103 M: Yeah even the stiffness I've found in my fingers has disappeared. Now I don't know
104 whether that is down to the medication, but it seems rather peculiar that six weeks and
105 it's gone.

106 PC: Right, so are most of you on the tablet?

107 M: Allopurinol, yeah.

108 PC: No?

109 M: I'm on one a day. [yeah]

110 M: 300mg.

111 M: I'm on something else, I've got to tell you what it is.

112 PC: You're on something else, okay.

113 M: It's [7:31].

114 M: I'm on a dose of 300mg, I don't know if that is normal.

115 PC: Yes, that's the standard, yeah. So when you said erm...you don't know if it's the
116 medication...

117 M: Magic, absolute magic.

118 PC: Right. Right, okay, so you're on...

119 M: Is that Allopurinol?

120 M: No.

121 PC: You're on Alcoxia.

122 M: Because that didn't work for me, at all.

123 M: Is that the same thing or...?

124 PC: That's not the same as Allopurinol.

125 M: That is absolutely the magic pill. I'll tell you in a minute. Bloody fantastic.

126 PC: Yeah, so let's talk about the treatment, so you said, Alan, that you don't know if it's the
127 medication, did anyone explain to you that why you need certain medications at certain
128 times? [yeah] [no] Do you know why you're on these tablets?

129 M: No, they told me this was to reduce the uric acid content in the blood. [okay] Basically.
130 [right] So that's what I've been told. [right]

131 M: Allopurinol does that doesn't it? [yeah]

132 PC: Yeah, so that's when you've been told. [or not] Right, what do you mean 'or not'?

133 M: Well my I can tell you quite a bit but initially I - my left big toe just started swelling up,
134 no idea what it was. And it got quite - very painful, went to the doctors, as soon as I took
135 my sock off she went gout. [okay] without any hesitation she went 'gout'. So she
136 diagnosed me a pill, I think it was Allopurinol, and I took them for a few days, absolutely
137 nothing, it was excruciating, [8:47] just like Bill said, you can't touch it, it was agony, just
138 like - exactly like you described it, somebody you know [8:54] me with like a - so I went
139 back to the doctor again and I said - in the meantime I'd been onto NHS Direct, and the
140 one - Allopurinol is apparently an old pill, an old fashioned one almost, and the new
141 one's that one. So I took all the stuff into her, I said I'm not being funny here but can I
142 have this one please because this one seems to be the new one, and much better. So
143 she went oh, let's have a look at this gout stuff. So she read it all, quite you know...took
144 no notice of me for a while, oh that's interesting, never knew that. So anyway after

145 much ado she give me that, two days later, gone! Absolutely fantastic. [right] And it only
146 came back once again quite a long time after, and I'd saved a couple or three for going
147 on holiday just in case erm something happened on holiday, because I thought I'll keep a
148 few back, thinking...

149 M: Always save three.

150 M: ...if you're in Spain or if you're in some godforsaken land, you know, [right] and sure
151 enough we were on holiday somewhere and it started to come back so I fished them
152 out, clears it instantly. I can't think - speak highly enough of that pill.

153 M: It's interesting what you said because my medic said that Allopurinol can actually cause
154 gout to flare up again.

155 M: It didn't.

156 M: And they put me on a low dose for one week, 100mg, and then up to 200mg, and then
157 to 300mg. and I was told that if it didn't, you know, if I had any problems, any pain,
158 [yeah] to stop taking it immediately.

159 M: But it's interesting what you said about...

160 M: Do you take them everyday?

161 M: I take them everyday.

162 M: One every day, one a day?

163 M: One a day, yeah, 300mg.

164 M: 400mg, I take 400mg so...

165 M: Yeah well mine's only 100mg, I'm on 100mg, 100mg, I should have been 100mg twice a
166 day but I thought I'd sort of cut it down myself to 100mg. and I've done that for a long
167 time now.

168 M: Does it balance it, does it?

169 M: One seems to balance it, yes.

170 M: A friend of mine's on one for the rest of his life he said [yeah] and I think it's that one.
171 [yeah] but I just had the short - that just kicked - just knocked it straight off. [yeah]
172 Miraculously, I can't tell you. But what I'd been doing, little realising, erm...talking about
173 beer, the club I drink at on a Friday night, they'd got a special offer on erm [laughs]
174 Coors Lite. [phew...] anybody else? [no, no, no] [yeah] So when I got it I went back in the
175 club [11:03] and I'd said I'm killing me, the steward says I've got gout and I've been
176 drinking it and another guy at the other end of the bar says I've got gout and I've been
177 drinking it. So I don't know normally drink that, but it must be something to do with the
178 yeast, Coors Lite. [yeah] And also the off licence I go erm because I drink at home, erm
179 they'd got it on special and I'd been drinking at couple at home as well. One top of that,
180 all the other things that I'd found on NHS Direct, by a combination I'd been absolutely
181 obviously building up uric acid something wicked; sardines, oily fish, I was eating that of
182 a lunchtime thinking I'd have it instead of a sandwich thinking I was doing well, erm

183 Saturday night instead of eating crisps and all that I was getting a little tray of muscles
184 from the supermarket, muscles have got it. My wife had been getting...

185 M: All the things you like.

186 M: Ah ah, the wife had been getting asparagus from the supermarket because it was on
187 special that time of the year, erm for starters for our dinner; I'd been to a dining out job
188 where I over did it on the port quite a bit again and I was having marmite on my toast in
189 the morning...

190 M: Marmite?

191 M: Yeah, and all that is like put it all together, and it's...

192 M: You either like it or you hate it.

193 M: Yeah, you love it or you hate it don't you? Yeast, yeast...

194 M: No, it's just that I've never...coped with marmite.

195 M: It is interesting because...

196 M: Well it's a contribute...it's got - it's high in uric acid. So all those things, one, two, three,
197 four, five, six things I was doing without even knowing what I was doing to myself, and it
198 just...that was it.

199 M: But you know you say about Coors Lite, the first time I found that I'd got gout was erm -
200 and I was in America, in Houston, [oh right] and I was drinking Coors Lite. And I was
201 having a shower and I don't know if you remember soap on a rope, [yeah] I dropped it
202 on my toe [oh!] [ooh!] and my toe came up that colour [yeah] and I didn't know, I - and I
203 took some aspirin like you know to try and get away from the pain, but erm it took me -
204 because I was in America and to go to the doctor there you have to have an arm and a
205 leg cut off, you know, [yeah] [laughs]...

206 M: Well there must be something...

207 M: Well it's interesting what you say though, up until about 18 months ago I was a real ale
208 drinker, three or four times a week [yeah] I'd go out for a beer.

209 M: That's what I always drink, yeah.

210 M: And I - the worst attacks that I've had is since I've stopped drinking beer, I drink a fair
211 drop of red wine...

212 M: So do I, yeah.

213 M: ...you know, more than half a bottle, but I think the worst attacks have been recently,
214 this is why I was asking about whether actually straining your joints is a reason for a gout
215 attack.

216 PC: Yeah. Well there are studies which show that joints that have been injured through
217 sports or any other injury, or you've had surgery on that joint, that joint is more
218 predisposed to getting crystals depositing and hence gout occurring.

219 M: Well if you have it too long, if you leave it too long, don't the erm crystals calcify?

220 PC: Yeah, they do...

221 M: And then you need to have the joint erm...scraped?

222 PC: Erm well not...you can get calcification without gout crystals because there are other
 223 sorts of crystals that will [yeah] calcify as well. Erm and so the treatment for gout, the
 224 aim is to dissolve those crystals and that's what I wanted to ask whether anyone had
 225 explained to you, all of you, why you take certain tablets at certain points, or Allopurinol
 226 life long, has anyone gone through that because...[yeah]

227 M: No, no, not with me. [right] I was just put on them.

228 M: NHS Direct, I found out for myself basically. [okay] So the doctor didn't really explain it
 229 that well. Erm...she was more interested in reading what I'd printed off [right] NHS
 230 Direct. And I understand they can't know everything about everything, I'm not being
 231 erm that critical, but erm it was very interesting to read the NHS thing and look at my
 232 lifestyle over the last - the weeks leading up to it, and I thought, phew...

233 PC: Okay, so you find written information more helpful from you know...

234 M: Well that particular one, yeah, erm...[yeah] and I actually gave it - I was going to bring it
 235 but I realised I gave the whole lot to one of the other guys who'd got gout in the club
 236 and we'd all - the Coors Lite was a definite link. And it's different yeast I think.

237 PC: Right, right.

238 M: While we're on medication for gout, when I first started having these attacks, they
 239 prescribed the non-steroid anti-inflammatories [yeah] for me.

240 M: Yeah, I had them.

241 M: And that made it even worse I found, [did you?] I had terrible reaction to them, swelling
 242 of the [right] foot, [right] increase in pain levels. So I came off them voluntarily.

243 PC: Okay, and what about Richard and Mick, tell us about your treatment, how has that
 244 come about, have you had any problem?

245 M: Well I do like a - I've had it for 42 years, [okay] [crikey] so I've tried everything.

246 M: No, and I have tried to narrow it down to what foods cause it but totally without
 247 success, so what I - I got a - take cortisone, [okay], as soon as a I get a twinge, and it's
 248 usually in the left big toe [and me], I know now that that's gout, straightaway, so I take
 249 two cortisone, and one, that's three in the first day, and then one each day thereafter,
 250 up to a maximum of 12, because if you go more than 12 you get a nasty side reaction
 251 which I won't go into. [laughs] [well...] Yes, well you can say if you like. Yes.

252 PC: Okay, okay, so you mean diarrhoea?

253 M: Yes, I do. Yes. But I usually either three and then the one I'm - in 36 hours it's gone. It
 254 only takes four. [okay] And also I had a nasty reaction to Allin...

255 PC: Allopurinol?

256 M: I can't have a [17:01]...

257 M: Allopurinol?

258 M: Yes, I got muscle spasms, [right] not spasms, but they were weak. [right] Is that a
259 reasonable? Yeah, [yeah] yeah. So I'm now on - well I have been for years,
260 sulfinpyrazone, [yeah] and you start off one, [yeah] which is one, it's 100mg, and then
261 you do that for, I've forgotten now, it's such a long time ago I started, for a month I
262 think. [yeah] And then you go - and then you get gout, it gives you gout, and then well
263 only mild gout, not severe, and you go two for I think it's two months, I've forgotten
264 now, [yes] and then you go to three, and then that is - that's a miracle. [okay] Because
265 you don't get any then, but then you come - the doctor puts you back to two because
266 it's bad for your kidneys isn't it?

267 PC: Some people can get problems, yes.

268 M: Yeah so I'm on two now, and I've been on two for years, and I only get gout about once
269 every three months. [okay] And it's mild.

270 PC: Okay, right. What - what makes you, all of you, come off the treatment, is it just the side
271 effects or - or you know - or have you stopped because - stopped taking treatment
272 because you've stopped getting gout?

273 M: Mmm. I still take Allopurinol.

274 PC: You still take Allopurinol.

275 M: But I found that - I've actually found out what's caused my gout.

276 PC: What's that?

277 M: Dairy products. [right] [laughs]

278 M: No!

279 M: No.

280 M: Oh but...I don't think you - I honestly don't think you can narrow it down...

281 M: I can.

282 M: ...but then there's a theory, which I - that it's the change in diet that does it.

283 M: Well like I say it was 1976 when I first found I'd got gout when I dropped the blinking
284 soap on my toe.

285 PC: It's - it's, yeah, it's very different for different people, [yeah] there's some people - I've
286 heard the dairy erm story before but...

287 M: And I went to - it was a fair while before I got back to England and went to see my
288 doctor [yeah] and he said gout straightaway like, [yeah]. [yeah] And he said what you've

289 got to do is find - he said it's caused by purine in protein, he said there's something in
290 your diet that's causing it. [okay] And I've always been lactose intolerant.

291 M: I'd be interested to know, nobody has ever explained to me, can you naturally have a
292 high level of uric acid in your blood, and no matter what you do about it [yeah] you can't
293 reduce it, [yeah] a bit like...

294 M: Your body can actually build up acid can't it?

295 PC: Yeah so if you're not excreting, because there has to be a balance between the
296 production and how much you're chucking out, and if you're not chucking out enough,
297 or you're producing too much, that balance is not right, and [yeah] some people
298 genetically or you know inheritantly they produce more than others, and you may not
299 know or you may not have gout for years, you might have a high uric acid for years
300 before you get that attack, so it doesn't have to be, you know, you have high uric acid,
301 you'll get an attack tomorrow. Could be ten years before [yeah] you find out.

302 M: But can you have mild gout, the sort [yeah] that I was talking about, [yeah] where you
303 have constant pain in your joints, with the occasional, you know, sharp pain, when
304 you're - that stuff.

305 M: Constant, you mean all the time?

306 PC: Yeah, absolutely. Yeah.

307 M: Yeah an ache in the joint.

308 M: Oh I've never, never had that.

309 PC: You've not had that before?

310 M: It does go away after a while [okay], if you stop eating and drinking...[laughs] no, sorry,
311 that's a joke.

312 M: I think [20:34]

313 M: I mean in six weeks it's transformed the pain...

314 M: I never, in fact, I - I drink very little alcohol.

315 PC: So if you know that something's triggering your gout, do you stop eating that or drinking
316 that?

317 M: Well yes, and one time I was convinced it was white wine, but it isn't, it's - it seems to
318 change over the years what triggers it. Perhaps as you get older it's different things.

319 M: I know - to be honest I know - I know it's dairy with me.

320 M: Do you? You're lucky, you're very lucky.

321 M: I am, well maybe I am, I don't know. Just erm...[yeah] I used to - I used to go down to a
322 place in erm Southall, Crown Cork, you know where they make the bottle tops, [yeah]
323 and there was an old bloke there, an old Scots bloke down there working in the factory.

324 And erm he used to work in his slippers, his gout was that bad. [oh yeah] And I was in
325 the canteen with him, we were talking about - I said why are you wearing slippers, he
326 said the bloody gout mate, it's a bloody killer. [laughs] I said well, I said I get gout, I said
327 but you know I found that erm dairy products do me. Dairy products, he said, cheese
328 and all that? I said yeah. He said I have cheese on toast every night for my supper. I said
329 oh right, I said try knocking it on the head like, you know. It was only about a month
330 later he'd got his work boots on and he said you've saved my bloody life mate.

331 M: All I can say there, that person is very, very lucky.

332 M: Well I know I'm lucky to find, to know....

333 M: Yeah, because I was told it was cheese, and I eat a lot of cheese, but I stopped eating
334 cheese but I still got the gout.

335 M: Yeah but it's dairy products, you know, it's cream, cheese, milk.

336 M: Well I don't really...I...

337 M: I've - I've erm always eaten large amounts of sea food, mussels, prawns, oily fish, that
338 sort of thing [yeah], all my life, erm I don't eat as much as I used to, but I'm still eating it.
339 [right] And...it doesn't - I can't tie it down to eating.

340 M: Well I love king prawns I absolutely adore them, so if I have Chinese or an Indian [yeah]
341 it's always king prawns something, but that's not like everyday. But I was getting - I was
342 eating quite a few mussels and sardines as a sort of healthy alternative to crisps and
343 sandwiches and that, [yeah] thinking oh, I'm doing well here. I'm eating all the good
344 stuff, little realising that you're topping up with...

345 M: Had you stopped taking it and you think it is...

346 M: Well asparagus came and went because that was a seasonal thing, so - but we did eat
347 quite a lot, the one big dinner I had and I did have a lot of port that night. I stopped the
348 marmite straightaway, because I can do it. Erm...

349 M: Do you get - do you get - does anybody get reflux as well?

350 M: What do you mean by that?

351 M: Sorry?

352 M: Acid, you know, acid coming up?

353 M: Erm...occasionally, but that's...[no] [occasionally] you mean like the bile?

354 M: Where it burns the bottom of your...?

355 M: Heartburn?

356 M: Occasionally. Yeah.

357 M: Ah, very bad heartburn.

358 M: No, I don't get that.

359 M: But a lot of people get that you know.

360 M: Is that indicative of gout?

361 PC: No, not particularly, no.

362 M: Somebody told me it was a sort of...

363 M: Obviously the Coors Lite, that stopped straightaway, and this little baby, I can't speak
364 highly enough.

365 M: Can I just say what I'm on.

366 PC: You're a big fan of that tablet?

367 M: It's absolute magic. [right] Magic. Erm...

368 PC: Do you just get that off your doctor whenever you have an attack?

369 M: Yeah well I've only ever - erm I think I've only had the one lot, and I kept a few [right],
370 erm because I don't know, I only got 14, [right] so I thought I'd - by the time I'd taken
371 about, it was one a day, by the time I'd taken three or four, [yeah] it was going down
372 really quickly, the pain had [yeah] gone, and within a week completely gone, the
373 swelling had gone down, and so I thought well I'll save some of these because if - and it
374 did come back, not as bad, [yeah] erm and I thought what am I doing, what am I doing,
375 so I got my little list and I thought no, no, no, it's just obviously something else.

376 M: You - do you take those when you feel an attack coming, or every day?

377 M: No, no, no, it's - it's months and months. When I first got them about a couple of years
378 ago, erm I had the other one, the...Allopurinol I think, and it didn't help at all and I had
379 to go back to the doctor with a massive pain and with the information and I said can I
380 have this one? [yeah] she didn't offer it because it's obviously more expensive, well
381 that's what...

382 M: But that's every day, you take one of those every day [yeah] for the rest of your life?

383 M: No, no, no, once I'd got it, it wasn't like before, or after, it was just...

384 M: So it's like what I take [24:57], it's the same.

385 M: It just stopped it. I don't have to take it everyday. I only took about four and it - and it
386 woo! Fantastic. [yeah, and that's it?] And then I kept some, as I say I went on holiday
387 and I thought if I'm in some far flung corner where you have to go and pay through the
388 nose, so I thought - and sure enough I did get a mild attack somewhere, I forget, we
389 were overeating, over drinking, as you do on holiday, erm and kept them in my pocket,
390 bang, two days later, gone again. And I've run out now so if it comes back I'll have to go
391 and get some, but it's only a very temporary thing, [yeah] I don't know whether you can
392 take them long term.

393 M: Yeah it's just like my cortisone, it's exactly the same.

394 M: And I can't speak highly enough of it, [no, I can't] for me personally that did it, it's
395 within...

396 M: And you've had no side effects?

397 M: No. within days, completely gone. Swelling goes down, pain goes, obviously breaks
398 down the uric acid, and as you say you get it, goes out through your system. We've all
399 got it, haven't we? [yeah] We've all got uric acid. But I must have built it up
400 unknowingly, with a combination of things. And then that breaks it down, stop doing
401 that, and it gets rid of it. I'm assuming that's right.

402 PC: So I just wanted to ask you about, so obviously the, you know, you think that treatment
403 works brilliantly for you, erm what do others feel about the treatment, do you think it
404 works? Doesn't work? How does it affect what you do every day?

405 M: Well mine works at the moment, I haven't had any - an attack for about six months now.
406 [right] I would say six months by just...

407 M: What are you on?

408 M: ...first of all taking Allopurinol, twice a day. [okay] And then I dropped it down myself to
409 one a day, I don't know what the doctor will say when I tell him but...

410 M: That's over a long period of time though?

411 M: Six months now since I've had an attack.

412 PC: Can I ask you Mick, sorry to interrupt, why did you drop it to just one a day by yourself?

413 M: Well I thought if two's doing all right and with not having any attacks, [right] I would just
414 try - I'll try and see what one will do. [okay] I mean I have even thought about trying one
415 every other day, and whether we can, you know...

416 M: I must admit I've had the same thought as I told you, that I started off at 100mg, and
417 after the week erm [yeah] there was significant improvement but I carried on up to
418 300mg.

419 M: So did they give you that much of erm a...erm...

420 M: Yeah after a week.

421 M: No, I mean did they give you a lot of pills then?

422 M: Yeah they gave me 100 pills. [wow!] 100x100mg pills, and I started off 100mg for one
423 week, 200mg the second week, and up to 300mg. and as I've had no erm...side effects
424 from it, they've given me two months supply.

425 M: And this was just two weeks? The ones before were I think one or two weeks again, but
426 there wasn't any long term you've got to keep taking it.

427 M: I must admit that my GP, he's very keen, I - I take medication for high blood pressure
428 and...

429 M: I do, yeah.

430 M: ...and erm complete control.

431 M: Ramipril, yeah.

432 M: And every six months we have blood tests, so I'm presuming they will continue with
433 those blood tests to make sure there's no side effects from the Allopurinol.

434 M: I have a blood pressure every six and a blood test every year. And she does different
435 things like liver, kidney, you can tick all the boxes can't you? [yeah] [yeah] So every cycle
436 of every year or two, I imagine I get everything checked. [okay] Especially the liver in my
437 case. [laughs]

438 PC: And so the treatment, what do you - so what's the main aim of it for you, what do you
439 want it to - you know, if it's not doing what it's meant to do, what you want it to
440 improve or how does it affect your life overall, what can you do without it or not do
441 without it? Or you know...

442 M: Well when I get an attack it's - it's quite severe, it's like - it's the one where you can't
443 have the sheet on the bed and I don't know about the bloke with the slippers, you can't
444 put your slippers on really. Erm you know he must have suffered...

445 M: You can't walk, you can't walk.

446 M: No. you can't walk, it's a sitting down job.

447 PC: So you feel quite disabled with it?

448 M: It's almost, well I've been where I've been crying with pain. [yeah] It's so...

449 M: It's indescribable.

450 M: It's distressing.

451 PC: It's distressing, and how does that affect - so obviously that causes you distress and how
452 does that affect other parts of your life?

453 M: Well the wife goes - the wife goes out and leaves you alone like, you know. [right]

454 M: I'm one of these people I can't sit still, I've always been active all my life. And it just stops
455 all of that. [right] Erm I get - I don't have the problems of you know you can't touch it,
456 but the pain is so severe you - you just feel you can't put your foot on the floor.

457 M: No you can't.

458 M: Erm...really, I've never had pain like it, as I say, just like a red hot poker being pushed up
459 sort of...

460 M: It's worse than tooth ache.

461 M: Oh oh.

462 M: I don't know, it's...

463 M: I very rarely get severe pain, very rarely. [right]

464 M: I mean at night I find it's the worst.

465 M: But you remember it. [yeah]

466 M: Yeah, because you're...

467 M: Well my wife has to go and sleep in the other room because she says if you don't shut
468 up, and I was going - because even if - you can't turn over, when you're half asleep, you
469 accidentally touch something...

470 M: You learn new swear words.

471 M: And erm [laughter] she's saying you'll wake the neighbours up if you keep on because
472 you're really crying out. [laughs] Crying out with pain.

473 M: Yeah and also you're frightened that she's going to touch it.

474 M: Well the sheet thing, yeah...it's oh...

475 M: Well this was a - why I was in denial. I could catch hold of my foot and squeeze it and it
476 wouldn't cause any problem, other than I knew I had severe pain [yeah] up through the
477 bottom of my foot. [yeah] I didn't have the - what I termed as being the classic gout.

478 M: Well I found - I found that if...

479 M: Is that the bottom of the foot?

480 M: ...if my wife manipulated my big toe, [phew...] I don't know - I mean I don't know if that's
481 what - what happens but it thought it would break down the crystals, but I didn't have
482 any extra pain.

483 M: Even if the next toe touches it it was like aahh!

484 M: Well she was sort of manipulating the toe.

485 M: That's interesting because - because of the all the problems that I had with my foot, and
486 I've got private medical insurance, I got referred to an orthopaedic surgeon in Oswestry,
487 and I went to see him, and I sort of had this sort of constant pain but it wasn't really
488 severe. He manipulated my foot, looking at it, within a matter of minutes I was in agony,
489 [ah] I couldn't move. [right] Couldn't move with it.

490 PC: And so, yeah...

491 M: So something that I do to my joints, I think, triggers something or other in my foot.
492 [okay] As I say, moving gravel, going up ladders in bare feet and things like that.

493 M: I've stopped doing it. [31:27]

494 M: I retired about a year ago and I'm more active now than I ever was and I've lost weight, I
495 play golf regularly, do a lot of walking erm far more than I did because I had a sedentary
496 job, I was a sales manager driving a car to meetings, so it was a real crap job for exercise.
497 And then by the time you get home your mentally stressed, all that sort of thing, so - but

498 now I've sort of made a definite put to have more exercise, and get out more and erm if
499 the gout came back that would severely affect that obviously. [okay] But it hasn't. only a
500 very mild one, erm so the worst one was like - it was like a sudden surge and that killed
501 it [yeah] and it came back a little bit, and as I say it killed it off again and touch wood it
502 hasn't come back.

503 PC: And what does it mean for you, you know, to have gout? If you met someone who you
504 know had recently been diagnosed with gout, what would you say to them? What
505 advice would you give them, about treatment?

506 M: Go to the doctors and get the pills. [laughter]

507 M: Straightaway, yeah.

508 M: Get that lady, quick.

509 M: As quick as you can.

510 M: Get the cortisone.

511 PC: Right.

512 M: And the - either the Allopurinol or the [32:29].

513 M: It's got another name on the back, if you make a note of it it's called etoricoxin [yeah].

514 M: Pass it over, I shan't - I won't be able to spell that.

515 M: Well it's not that, it's there in the back there, look.

516 M: I think my GP started to - to it when it was first started, this is why I asked whether
517 you've had access to medical erm records as to whether he had - he really had
518 diagnosed gout several years ago [okay], his attitude was a little bit well, if you're only
519 getting attacks infrequently [yeah] don't bother with the medication.

520 PC: Okay, that's interesting.

521 M: And from my perspective I had this constant pain which I could live with, it stopped me
522 doing the long distance walking, and the high impact sort of exercise, but I could live
523 with it. [okay] But it did alter my lifestyle. [yeah] And now I've been on these pills for six
524 weeks and my foot, okay, it's still stiff and a bit achey, but compared to what it was only
525 eight weeks ago, [wow] it's a massive improvement.

526 PC: So are you saying, Alan, you wished you'd gone on it earlier?

527 M: I think now, yeah. [yeah]

528 M: Is there a standard treatment for it? [yeah] For like a standard nationally? [yeah] Is it the
529 Allopurinol that's standard?

530 M: Erm it's one of the standard treatments, but it's so - that's what I was trying to get out of
531 all of you, whether you know the difference between treatment in the acute phase,

532 when it's red hot, sore, and Allopurinol which normally is started later on when the
533 attack settles, and that's the long term...

534 M: When my - the doctor gave me some pills that if it is gout I get erm diclo...I can't
535 remember now.

536 PC: Diclofenac?

537 M: That's it, yeah, Diclofenac.

538 M: Yeah, yeah.

539 M: And when it goes like, you know, erm swollen up [yeah] I take a couple of those and it
540 goes down. [okay] But I haven't had any - I haven't had one of those for ages. I've got to
541 - [right] I've got a little bottle full which I always in mind like, you know.

542 PC: Do you know about any other treatments apart from these tablets that we've talked
543 about?

544 M: I only know about Allopurinol.

545 M: You can put it...

546 M: Except what I've read on the NHS site, sorry.

547 M: ...well I have tried - I have tried this, you can put it in water, [okay] which relieves the
548 pain. And the trouble is I have a friend and he always puts his in warm water, and I tried
549 cold water. [okay] So there's two different things straightaway. [okay] But it's so
550 awkward sitting with your foot in cold water.

551 M: Surely cold would make it worse though?

552 M: Erm no, I use cold water, it does - if you get a severe attack it does make it better.

553 M: Really?

554 M: But the trouble is, you're so bored sat there not being able to move your foot, [laughter]
555 that you get psychological side effects.

556 M: Because what I read in the...

557 PC: That's interesting.

558 M: ...going back to the NHS again, these crystals are in your blood travelling around your
559 body and the coldest spots, which tend to be your toes, [yeah] they will sort of
560 crystallise there.

561 M: Yes, farthest from the heart.

562 M: So I've just had the one left big toe, no other toes, no other joints, nothing, and it fell in
563 to the exact sort of erm condition what they described as being furthest away you know
564 and therefore the coldest [yeah], but I would have thought cold water would actually
565 exacerbate it.

566 M: Well I have tried warm water as well and that's not...

567 M: I don't know, I'm just - it's interesting to...

568 M: That is another treatment you can try.

569 PC: Yeah, so different things...okay. Yeah.

570 M: But it's only relieving symptoms for a little while.

571 M: Is that because it's numbing it do you think?

572 M: Yeah possibly, yeah. Yeah. Erm but...

573 M: It's interesting actually.

574 M: Yeah but there is - you can have injections of cortisone because it's like arthritis isn't it?
575 [right] I have never got to that erm stage. But my son gets it and he gets it worse than I
576 do. I know I shouldn't speak about another patient, but he has been treated at the
577 Haywood. [okay] And his is so severe that his immune system attacks his body, this has
578 only happened once. And he swells at every joint. [dear!] Yeah, I don't want to alarm
579 you because it's very rare apparently.

580 M: No, it's just - it's not that erm...my daughter's got this erm symptoms of erm gout, and
581 she's been going to Derby to erm - erm - because my other daughter has got erm -
582 what's that carpal tunnel thing, she's had to have an operation. But she's - this other
583 daughter, she's erm come up, as far as I know, in her foot and all that like, you know,
584 and I had a look at it, and erm I think the way it is and all red and raw and painful, I said
585 it's flipping gout. [okay] And she's having treatment for all sorts of things like, you know.
586 So it could be where she's got gout and [right] and...

587 PC: So yeah, it's interesting then that you mentioned family members having it.

588 M: And my mum had got gout. [right]

589 M: Is it true though that women don't - have far more rare, far more less likely to get it than
590 men?

591 PC: That's really interesting.

592 M: That's my experience, because most of the people I know who's got it are men.

593 M: Are men, yeah.

594 M: I don't know any woman who's got it.

595 PC: No.

596 M: My mother in law got it.

597 M: You're the first two people who have mentioned women.

598 M: But she was 80 odd before she got it.

599 M: You don't brag about it do you? [laughs]

600 PC: You don't brag about having gout?

601 M: Having gout, no.

602 PC: Why not, what's so...so what stops you talking about it?

603 M: [laughs] There's this little stigma.

604 M: Well you don't brag about it, but...

605 M: It's self denial, you think it's an old man's...[yeah]

606 M: Everyone laughs at you, when I first said it in the club...

607 M: Eating too many pigeons.

608 M: ...everybody laughs and says oh...too much rich food.

609 M: Too much capon and erm...

610 M: ...and you're drinking too much wine.

611 PC: Yeah so what do other - so if you tell your friends, what do they think, or your family,
612 what do they think about it?

613 M: Oh the first thing they say is too much red meat and too much port.

614 M: Oh my wife's had - my wife's said everything. It's everything I eat that's doing it. [right]

615 M: I went for my tablets to the chemist, [yeah] and erm the lady at the chemist said erm
616 her father suffered with gout and he kept off red meat, tomatoes, oranges, orange juice,
617 and those things, so I - I like T-bone steak, [38:26] so cut out T-bone steaks, in the last six
618 months or so...

619 M: But how often were you having it?

620 M: Well I had one regular every week. At least one a week, [right] [okay] I used to get three
621 or four from the butchers and put them in the freezer. [yeah] When he'd got them, you
622 know, when they looked good.

623 M: Yeah, off a good cow.

624 M: So - so I - I've cut them out, so I don't have them at all and we're eating more in the
625 chicken side of erm food rather than [yeah] - rather than the meat. But I...

626 PC: So yeah, it's interesting, yeah, go on, sorry.

627 M: Pork, pork was the other thing, you know mentioned pork, I didn't think pork was as
628 bad, I don't think pork is as bad, because that's the other meat that we've sort of gone
629 instead of red meat, pork is not as red meat, it's...as that, so I...I tend to go for pork.

630 M: It didn't - and I'm going back to NHS Direct, I keep on about it, but it was - I was really
631 interested to read it, it didn't really go on too much about red meat, and red wine, it
632 said - which is - I thank my lucky stars because I do like red wine, it said red wine has not
633 been proven to contribute to gout in any way, but port does, which is a bit odd because
634 it's fortified red wine isn't it? [yeah] But I did, you know, erm I told you what happened
635 to me and [39:39] I was building up uric acid like crazy without realising it.

636 PC: So it's interesting, all of you have talked about what sets it off and food quite a bit, erm
637 you know is that - so that's - would you say that's the main thing you modify to prevent
638 an attack? [yeah] Rather than relying on tablets?

639 M: I haven't modified my eating habits at all.

640 M: Definitely with me.

641 M: But I think I've got a balance, you know, between white meats and...

642 M: It's all moderation thing isn't it I suppose?

643 M: What I am more aware of is don't stress that joint. That's the thing that I'm [okay] very
644 careful about now.

645 PC: Do you...

646 M: One thing it definitely causes for me...

647 PC: Sorry, say that again.

648 M: One thing that definitely causes it for me, it is lites, the liver or kidney. [right] So I
649 haven't touched that for years and years and years. [okay]

650 M: It's - it's odd isn't it because you know I love it...

651 M: And grapefruit.

652 M: Grapefruit, yeah. [40:32]

653 M: I mean I've heard of strawberries even.

654 M: We're not supposed to take [40:35] with a lot of pills are you?

655 M: Because anyway with statins you don't erm...

656 M: There's a lot of antibiotics and pills that you should - because my missus is on different
657 courses for thyroids and [yeah] god knows what, and if you have grapefruit which she
658 used to have half a grapefruit in the morning for breakfast, and grapefruit has for some
659 reason a severe erm reaction with lots of pills. [yeah]

660 M: Oh well, I haven't taken it for four years so...

661 M: It does, yeah.

662 M: I don't know why, because I mean it's - why all that should be more than say oranges,
663 because of citric acid, whether it's a different kind, I don't know.

664 M: When I say I haven't changed my eating habits, I've done one thing, [yeah] I'm drinking
665 cherry juice most days.

666 M: Cherry?

667 PC: That's interesting. Right.

668 M: Is that - I have erm...

669 M: Because I don't know if you've been on the site...

670 M: I have cranberry, cranberry every...

671 PC: A lot of people have talked about that actually, erm does it...

672 M: Whether or not it's having any effect, or not, I don't know.

673 M: Why did you do that then? Is that...

674 M: Because I - on the internet looking round for...

675 M: Oh right, I didn't see that. And erm there is a site on cherries and its affect on gout.
676 [really?]

677 M: A guy I know...

678 M: Particularly gout then?

679 M: Absolutely, yes. Yes, there's a lot of [41:37] about cherries.

680 M: A guy I know has got gout, and he has five cherries every day.

681 M: Apparently if you eat 2lbs of cherries a day, it keeps the gout away.

682 M: That's what it is.

683 M: Must be something in that then.

684 M: That's one of those things, so cherries, and cherries, I love to have cherries.

685 M: If you go on the internet on gout and cherries...

686 M: Oh I must have missed that.

687 M: ...and you'll - there's a whole - well, there must be about 20 different sites talking about
688 the effects.

689 M: I've actually bought a cherry - I've planted a cherry tree about two years ago, I'm waiting
690 for some fruit to come off it now. [laughs]

691 M: Well Sainsbury's have started selling pure...

692 M: Put a net over it. [I did] The blackbirds will have them.

693 M: Sainsbury's have started selling pure cherry juice recently, so [okay] whether that's...

694 M: I think it's nonsense because I did a course of that, eating 1lb, I couldn't afford 2lb, you
695 try eating 1lb of cherries a day.

696 M: Yeah but it's [42:20].

697 M: And I got gout.

698 PC: So that's interesting though that all of you - you obviously you know...come up with your
699 own ways of keeping it at bay and [yeah] you've said [you have to] you've looked at the
700 internet, NHS or you know cherries and gout, whatever, have you discussed this with
701 your doctors as well? [yeah] Do you go to your doctors about this sort of thing or do you
702 just do it yourself, look on the net?

703 M: Well when I told - when I told my doctor that dairy products caused the gout he said
704 what are you flipping on about? [right] He - he said you're daft. [here, here]

705 M: I think the erm...

706 M: I said all right then, if I eat cheese or the missus makes a cream cake and I eat that, gout.
707 You know.

708 M: I would say my GP almost dismissed my view that [yeah] the attacks were brought on
709 when I stressed the joint, but on the NHS site, definitely it states [yeah] that if you stress
710 a joint it can instigate the gout.

711 M: It's more likely to, yeah.

712 M: Well I know this - that wrist was shattered, that thumb was shattered, this little finger
713 was shattered, my elbow was shattered, and if I get a really severe bout of gout they all
714 swell up. [right] That arm becomes almost useless like, you know.

715 M: What was that in Mike, a road accident?

716 M: No, on the rig, erm a high pressure hose blew up, lashed me.

717 M: It's - I've never been severely injured but it's - it's very interesting that it attacks the
718 joints that have been injured.

719 M: Well arthritis does that.

720 M: The doctor said that the joint was smashed into eight pieces and he says all them like
721 little bits like, you know. [right]

722 M: But the last severe attack I had, where they took my little toe off, and I think at the time
723 they said I had something like [44:08 - Sweden] gout or something, you know, erm I
724 could feel the pain migrating to that joint, the remaining joint.

725 M: The remaining erm...

726 PC: Right, and how do you think we can sort of improve the understanding of gout for
727 patients, relatives, doctors or you know how sort of understanding gout and its
728 treatment? Do you feel that...?

729 M: Well take us seriously.

730 M: Well hopefully they can get it and then they'll know. [laughs]

731 PC: Hopefully get it, right, okay. [laughs]

732 M: Then they'll know what to do about it.

733 M: You tell somebody and they think - they think you're exaggerating don't they? [yeah] I
734 can't describe the pain and y all have toothache...

735 M: It's a good job the body doesn't remember pain.

736 M: No, it is, it is. Yeah. [right]

737 M: But I think the diet, I think your last statement, I think being aware of your diet and
738 moderating things that are likely to bring it on, which is what I did, erm and I looked at
739 what I was eating and that combination was - was relatively temporary that I was doing,
740 so obviously I could knock things off without really affecting my lifestyle, like the Coors
741 Lite was just because it was cheap basically that's why we were all drinking it, because
742 they had it on offer. So that came and went. So I wouldn't normally drink it, but it was
743 like £1 off a pint or something. Erm and the oily fish and other things, I still eat but in
744 moderation. So I was like combining it [yeah] so I like king prawn, I love shellfish, erm
745 but in relative moderation. And I think the dietary thing is probably one of the most
746 important things to be aware of yourself, erm but you don't know that you're liable to it
747 until you get it, so I didn't know [yeah]...

748 M: But the doctors - the doctors don't - they just say oh, you've got gout, and they just give
749 you a pill.

750 M: Well that was it.

751 PC: So they don't tell you about what to do with your diet, is that what you're saying?

752 M: No, I had to do that myself.

753 M: Yeah, they don't, yeah.

754 M: She didn't say a thing.

755 M: Is it the same as with the statins, will we get to a stage where you'll be recommended
756 when you get into your 40s to go Allopurinol, to keep the uric acid level low in your
757 body?

758 PC: Right, right, okay.

759 M: As you do with statins, to keep...

760 PC: So you think it's becoming that common that it'll reach a point where people will just be
761 given Allopurinol like people get statins, which is very common these days.

762 M: Yeah.

763 PC: Right, okay, that's interesting.

764 M: Well I'm asking the question basically.

765 PC: Okay, I don't think it will come to that, because you know studies have proven that by
766 reducing uric acid you are reducing the sort of end effects of high uric acid, like kidney
767 damage, erm and there's no way to predict who's going to get gout if you have uric acid
768 you can't - I might have high uric acid, I don't know if I'll get gout. There's no way to
769 predict it.

770 M: No, you're much too young.

771 PC: Well, oh you'd be surprised, so you think only older people...?

772 M: [46:55] babies, actually babies can get gout.

773 M: I think you have to be in your 40s like Alan just said.

774 M: No, talking of [46:59], I've just remembered, a friend of my daughter's who was anorexic
775 didn't drink, hardly ate anything at all, was about six stone dripping wet, and she was
776 like 22, 23 years old, she got gout. [ah!] And it was like how the hell, when you think of
777 the diets we've all talked about, and the foods and the overeating and drinking and one
778 thing and another, [yeah], she got it and she's about 30 now. And erm...

779 M: I think there's a lot of nonsense, not nonsense, a lot of myth...

780 PC: No, that's fair enough.

781 M: ...about the food because over the 43 years I can - I've only put it down to the kidneys
782 and the erm...liver and oysters. [ah] But only because I eat over eight oysters and got a
783 severe attack. But I think everything else depends on your, that person's metabolism.

784 M: I think you're right to a point.

785 M: And you know you can say that cherries, some people say cherries are good for it, others
786 say that's bad because it has purinol, they have purinol in them. [okay] And I've seen
787 tons and tons of things written and heard them about gout and it's just a great muddle
788 about when it comes to food.

789 M: It is actually yeah, you're right.

790 M: Well it's a muddle about a lot of things isn't it? Medical...

791 PC: Yeah, so what other things do you think is myth about gout? Yeah, go on then.

792 M: Well since I've changed my diet erm my cholesterol has gone down two points from 6.5
793 to 4.5. [yeah] So whether that's with not eating the red meat and...

794 M: Mine's gone down with certain diet changes.

795 M: The last time he took a blood test.

796 M: Does cholesterol have anything to do with gout?

797 PC: Sorry, say that again.

798 M: Has cholesterol got anything to do with gout?

799 PC: That's interesting. I was going to ask all of you the same question actually, do you think
800 there are other associated conditions that predispose you to gout or cause gout?

801 M: Well my cholesterol is lower now than it has ever been erm because I take a statin
802 [right] erm but I've - over the last two years started having these attacks of gout. So...

803 PC: Okay, so you think it's not related?

804 M: No, I don't think it's related.

805 M: Well mine was high but it got...

806 M: I don't think it's related. My cholesterol is - my natural cholesterol is very low, [okay]
807 everybody has a natural cholesterol level [yeah], and you can reduce that to make - but
808 mine reduces to 1.6. [wow!] Yeah, I know. [bloody hell] But you shouldn't run below
809 that, should you, because it's a bit dangerous. [no]

810 M: [49:24]

811 M: But I - it runs at 3.2. And by taking a statin you can halve it. [yeah] SO your risk of heart
812 attack, stroke, is halved. Whatever - if it was 10 and you halved it to five, it would be the
813 same. I mean - so you may run at a cholesterol level of eight, [yeah] if they're saying
814 what I think, I don't know, I haven't got a medical degree, but I think it's the same with
815 uric acid. As far as I can see you have a natural level.

816 PC: You do.

817 M: And if your level is high, you're more propensity to get gout. [yeah] And why that should
818 be more men than women, I have no idea.

819 PC: Okay, okay.

820 M: But you know better than I do don't you?

821 PC: Yeah, I'll - I'll - we'll answer those medical questions at the end, but erm...[yeah] just - so
822 that's, yeah, okay, and your doctors haven't sort of said to you, you know, there are the
823 conditions that could be linked to gout or we should manage those along with gout,
824 nothing like that?

825 M: Only hereditary. [no]

826 PC: Only hereditary, okay. [yeah] Right.

827 M: Well I see the nurse more than the doctor, just on the blood pressure and erm blood
828 tests and things, erm so unless there's something drastic which isn't very often, or very
829 rare, I see the doctor, so we have this sort of well clinic and [50:40] erm and she just sort

830 of mentions dietary things, erm so I've got a blood pressure pill and highish cholesterol,
831 but I've then changed my diet once again and that's brought that down without any
832 pills. But the wife's got, like I said, she has to have a pill for all that, erm statin is it?
833 [yeah]

834 M: You wouldn't have - I don't think it would do you any harm to have a statin, if it halves it
835 to two, that would be beneficial for you. [yeah] Or [51:07].

836 M: The - they erm threatened me with them, [laughs] if you don't get that down you'll be
837 on statins.

838 M: There are some benefits from Allopurinol as well, erm cancer of the...

839 PC: Well it reduces your cardiovascular risk erm so stroke and heart attacks.

840 M: It does?

841 PC: Yeah it does, by lowering the uric acid. So...

842 M: I had a - I had a - you know you were talking about cardiovascular, I had erm a letter
843 from the GP [yeah] and about erm abdominal audio something to check your heart.

844 M: An echo?

845 PC: Echo?

846 M: Yeah, something like that. Do they do from here or something?

847 M: Yeah.

848 M: They just brought it, it's a new thing like.

849 M: Oh you've just got to 65 have you?

850 M: No I'm 75 now. [oh!]

851 PC: No, it's...

852 M: A recent check, that's what you're talking about?

853 M: Yeah I thought [52:03] said they...

854 PC: Was it a jelly scan?

855 M: Jelly scan for that, aneurism.

856 M: Aneurism, that's it.

857 M: Oh, that, yeah.

858 PC: Right, right, okay.

859 M: They did - is that sort of related?

860 PC: Related?

861 M: Related to that? [no] Not to out but to cardiovascular?

862 PC: Erm no, no.

863 M: It can be if you have high blood pressure can't it, it can cause a swelling of the aorta.

864 PC: Yeah I mean it's basically dilation of the blood vessel.

865 M: As I say if they can keep you alive for another 100 years. [laughs]

866 PC: It's common as you grow older because your blood vessels aren't as erm you know
867 elastic, [stretchy] yeah well, so they stretch and then they don't go back. Erm but there's
868 levels so you need monitoring if it goes beyond 5cm.

869 M: Mmm, just wondering if they tied in with this. [no]

870 M: It's not [52:47] it's interesting.

871 PC: No, no.

872 M: But I have a heart condition. [okay] But I'm pleased to think it doesn't affect the gout, I
873 never thought it has, but...

874 PC: Yeah I mean it's...

875 M: I never thought of it like that with the other pills. [yeah] I've got ramapril just for blood
876 pressure, 10ml a day. Erm...that's...

877 PC: You don't associate it, you don't associate it?

878 M: I never give it any link. I didn't read anything that said that links it but I don't know.

879 PC: Okay, okay.

880 M: I'm on 11 pills a day. [11?] [right]

881 M: You rattle when you walk then?

882 M: I do, I do, yeah.

883 PC: So, yeah, and that's interesting that a lot of...

884 M: Well 10 and the gout one.

885 PC: Right, right. And does that do you think the other treatments for whatever other
886 conditions you may have, affects your treatment of gout or does your doctor treat you
887 differently because you've got other...?

888 M: I've never found that, no. I've never had a new pill and had an attack of gout within
889 three or four days, never. [no] So I don't - in my mind it's not associated.

890 PC: Okay.

891 M: My kidney function, he always checks because I think it's on the border line, so I think
892 that might have been one of the reasons he was a little bit wary about erm prescribing
893 Allopurinol.

894 M: Is that because of the side effects of that, of the Allopurinol?

895 M: Yeah.

896 M: Oh right, okay. Or possible side effects.

897 M: Possible side effects.

898 M: As far as I'm concerned...

899 M: But at the moment I'm going along with it, the relief in pain [yeah] is so...

900 M: It's worth the side effect, yeah.

901 M: Well if in six months time my kidneys are...not functioning very well I'll have to rethink
902 about it.

903 PC: Yeah. They'll probably, erm well I should be asking you this really, erm I was going to say
904 they'll probably send you to the specialist IUS at the Haywood, but - so have you, all of
905 you, had any experience of care in the secondary, you know, a secondary care hospital
906 setting, specialist or is it mainly managed by your GP? How does it work for you?

907 M: GP for me.

908 M: GP.

909 M: GP for me.

910 M: Well she didn't really manage it, she just - erm I went back and found that on the
911 internet, erm asked for it, she gave it me and it cured it, so there was no advice or
912 anything of that kind. Erm and I self regulated my own diet. [okay] Erm and the little
913 experience I've got, erm that's magic.

914 PC: Right. And what do you want the treatment to, you know, what should be the final aim
915 or the - the expectation from your treatment? Apart from obviously we've talked about
916 the pain side of things, is there anything else that you wanted to achieve?

917 M: Well it could be [55:32].

918 M: Non recurring.

919 M: It's down to your kidneys isn't it? They're out of balance aren't they? That's what it is.

920 M: You don't want it to recur basically, simple as that.

921 M: The kidney transplant is obviously out of the question.

922 M: It affects your lifestyle doesn't it?

923 M: Big style. [yeah]

924 M: But it's treatment of the kidneys that's the crux of the matter isn't it?

925 PC: Erm not quite, with gout. The crux of the matter is getting the uric acid out of the body
926 or [yeah] suppressing the over production of uric acid. [yeah]

927 M: Is it - is it a modern - modern disease? It isn't a disease is it, is it a modern...?

928 M: No, it's ancient.

929 M: No, it's ancient.

930 M: I mean you can see the old bloke with a foot up like.

931 M: [56:03] But I mean is it getting more prevalent in modern society, that's what I meant by
932 the diet we eat and all that?

933 PC: Yeah, yeah. That's interesting and so I want to just go back to what you said, it isn't a
934 disease, what do you mean by that?

935 M: Well, it's a condition. [okay]

936 M: Well with that, arthritis is a disease isn't it?

937 PC: Yes, well...

938 M: It's a form of arthritis in one way.

939 PC: So what's your differentiation between disease and condition, what do you mean?

940 M: For me, disease is something like malaria and erm...

941 PC: Okay, like infectious.

942 M: Infection like, yeah.

943 PC: Right, right, okay.

944 M: But it isn't is it, it's just a build up of stuff that's naturally in your body.

945 PC: No, gout's not infectious. Yeah.

946 M: Or unnaturally.

947 M: Well, it's there isn't it? I mean your sweat contains uric acid. [yes] [56:55] have got uric
948 acid haven't they? Your - if you're...if you've got a high...

949 PC: That's - that's - yeah, interesting actually.

950 M: What does uric acid actually do as a natural function, if it's in its correct level in your
951 body, what does it actually do?

952 PC: It doesn't do anything. There's no...

953 M: So why...? We get rid of it, and it builds up in the food we what, but it's already there...

954 PC: It's just a breakdown product of the body's metabolism.

955 M: Yeah so it doesn't have a function of, oh right, I didn't know.

956 M: And it's excreted to the kidneys?

957 M: Yeah.

958 M: Yeah we wee out basically, but if you've got too much then you still keep weeing it out
959 but there's still too much in your body, from what I can...

960 PC: Or you're not weeing enough out might be the other thing.

961 M: That's why erm...

962 M: One of the interesting things is that I've got a lot of faith in my GP, the way he's
963 controlled my blood pressure, etc. but he's never advised me to change my diet. [okay]

964 M: But he did in that - in erm - I was in the Navy, in the Royal Navy, erm...

965 M: So was I.

966 M: Pardon? [so was I] Was you, oh. And erm survival, some of the survival things is about
967 the amount of water you drink in a desert and places like that and in the erm cold
968 climes, but the amount of water...

969 M: I never sailed into the desert. [laughs]

970 M: ...the amount of water you drink, erm and controls the effect on your body. You can
971 actually die if you don't drink obviously, but erm what's happening to your body and
972 you're supposed to check your wee everyday. [colour?] Colour. [yeah, straw]

973 PC: So I mean drinking water will flush out, is that what you're trying to say?

974 M: Yeah, I'm saying you know you have to control, as part of your survival whatsername
975 that you check the colour of your wee. I'm sorry...

976 M: Yeah, no.

977 PC: No, that's all right.

978 M: Some erm gents you go in have actually got charts on the wall, have you seen them?

979 M: No, no.

980 M: Yeah, it says - and you're having a wee, and...

981 M: Oh you ignore those. Gosh.

982 PC: We don't have them in the ladies.

983 M: Well no, you're stood there and you're thinking and you look at this thing, what colour is
984 your wee? And you think oh right.

985 M: Well I ignore that, it just makes you worried because it's not the right colour.

986 M: [58:57] because when I was at - when I was working I used to drink an enormous
987 amount of tea, my fluid intake was huge; I don't drink so much since I've been retired
988 because I'm out doing things.

989 PC: Right, and so are you saying...

990 M: And I'm just wondering there is a link between...

991 M: Well all this thing about so many litres of water, just recently erm incidentally I read
992 somewhere where it's a bit of a myth because your body is a very clever bit of kit and if
993 you drink alcohol or tea or coffee, the body will take the fluid it needs and get rid of
994 what it doesn't need. So it doesn't have to be like eight litres of water a day or whatever
995 the figure was...

996 M: Eight litres!

997 M: Well, whatever it is.

998 M: Oh please!

999 M: Whatever it was, I don't know. [laughs] My daughter's manic on are you drinking enough
1000 water everyday?

1001 M: I know, mine's the same.

1002 M: I say well, going back to the wee thing, is well the colour's all right except if you have a
1003 heavy weekend, you know, and then [laughs] but erm...

1004 PC: Okay. So yeah...

1005 M: Yeah there was an article in the paper the other week and it said erm above seven cups
1006 of tea was bad for you, above seven cups of tea, [okay] well I drink about seven pots of
1007 tea. [laughs]

1008 M: Well then you get another one that says it's good for your - it's good because it's got
1009 antioxidants in it and...

1010 M: Yeah, I drink seven pots.

1011 M: So what the hell are you supposed to believe?

1012 M: You don't look too bad.

1013 M: No. I have it black, I don't drink milk with it, just tea. [tea?] No sugar, no...

1014 PC: Do you mean in terms of...?

1015 M: Tea, yeah. Well I drink - I drink lemon tea, so...[yeah] and coffee. No sugar, no...[okay]

1016 M: If I haven't got the pain of gout I'm going to eat and drink what I want.

1017 M: That's where you're getting your gout, from the lemon.

1018 M: From the lemon? The lemon.

1019 M: [60:28] I'm at the stage in my life, as long as I haven't got the pain, [yeah]...

1020 PC: So as long as you don't have the pain you will carry on...? [yeah] So you'd rather have
1021 tablets and control the pain and lead a normal lifestyle?

1022 M: Normal...

1023 M: Quality of life.

1024 M: ...quality of...

1025 M: Absolutely.

1026 PC: So that's what I was going to bring you [bloody right] all round to, thank you for bringing
1027 up that word, quality of life. [yeah] Now how has that been affected since you've been
1028 diagnosed with gout?

1029 M: Well you're just aware of what it can do to you if it comes back so the last thing I want,
1030 personally, is that to come back and affect the quality of my life because I'm getting
1031 more exercise, I'm enjoying life, I'm retired, I've got a really good sort of lifestyle, erm
1032 and that would severely affect it if it came back.

1033 PC: So...

1034 M: I mean when I have a severe gout attack, [yeah] it probably takes - and I haven't had it
1035 as bad as I don't think as some of the people round here, but probably it takes six weeks
1036 before I'm walking on my foot and feet with a level of pain that is bearable, I sort [oh
1037 gosh] - I'm sort of like this. [really?] [that's bad]

1038 M: You've got to be quick and get the tablets. [yeah]

1039 M: Well this is why I've...

1040 M: As soon as I get one bit of pain...tablet.

1041 M: That's right.

1042 M: You should get rid of it between 36 and 48 hours. [yeah]

1043 M: Well this is why I say, that having been put onto this - at the time I, you know, I thought
1044 it was a sprain and things like that, [yeah] but I - I'm - it's obvious it wasn't.

1045 PC: What other aspects of life does it affect? Obviously pain, activity, exercise, what else?

1046 M: Well your relationship.

1047 M: Never forget your pills.

1048 M: Your relationships a bit because obviously [laughs] according to my missus...

1049 M: Wherever you go.

1050 M: ...we're big moaners so...

1051 M: It's coming down to sex again, aye.

1052 M: A bear with a sore head comes to...

1053 M: You've got erm...it can get a bit stressful at home because if you're in pain and it's one of
1054 those that can't really - unless people have it, erm you don't always get the sympathy
1055 that - that you might think you ought to get. [laughs] You know.

1056 M: Yes, that's very good. [yeah]

1057 M: We do a lot of dancing, we go dancing about five times a week.

1058 M: Five times a week! Good god.

1059 M: So we, you know, that affects it if you get - if you get that pain then there's no dancing.

1060 M: You don't dance.

1061 M: No, yeah.

1062 M: Because you can't [62:41].

1063 M: Absolutely not.

1064 M: You can't change your shoes.

1065 M: Is that line dancing?

1066 M: No, no. erm...sequence dancing. Ballroom. Sequence. Sequence dancing.

1067 PC: Right, wow. And what about the treatment, how does that affect your quality of life?

1068 M: Well it improves your quality of life.

1069 M: Not at all, because...

1070 PC: It gives you the quality of life?

1071 M: It gives you a quality of life.

1072 M: It's just popping the pills isn't it? [yeah]

1073 PC: And you don't think that affects...?

1074 M: Well I keep going back to that, but after two days you know an immediate change, cuts
1075 down the pain, after three to four days the swelling is going down and that's it, end of
1076 story. [yeah] Bang, back to normal.

1077 PC: So you don't think treatment has a bad effect on quality of life, like gout itself? You think
1078 it improves...?

1079 M: It improves.

1080 M: Yeah but I've never got any side effects, I've never had any.

1081 M: I've got two border collies that I walk every day, when I'm suffering with the pain it's -
1082 just to get round is a strain.

1083 M: But you're on about side effects aren't you?

1084 M: Now, I'm fine.

1085 PC: Okay, yeah, well I just wonder if it's, you know, improving your quality of life,
1086 [absolutely] treatment is good, why do people not take it then, why don't they take gout
1087 tablets?

1088 M: Well you don't know you're going to get it until you've got it. And when it came back I...

1089 M: If they don't take it then they're in denial.

1090 M: Yes, that's a good point.

1091 PC: So yeah, why do you only take it when you're - when you have an attack, why don't you
1092 take it every day to keep it away?

1093 M: Well the doctor never said that I ought to.

1094 M: He's cutting his down.

1095 M: A lot of people do, I mean...

1096 M: Yeah I've been...

1097 PC: Yeah, why have you cut it down then if it's good?

1098 M: Well I've been fine for six months now.

1099 M: He's balancing it aren't you? [okay] You're balancing it aren't you?

1100 M: I did have two a day.

1101 M: But you're on a tightrope aren't you?

1102 PC: Right.

1103 M: It was some while since I'd had it, and then about six months ago, and the doctor
1104 decided he put me on these two tablets [64:25].

1105 M: But the GP wouldn't like it, well mine wouldn't, if you changed your dose unilaterally.

1106 M: He probably wouldn't.

1107 M: He's shouted at me recently and he's said don't leave off a pill or do any change unless I
1108 say.

1109 M: So why did they come to the decision that you had to take something every day for
1110 presumably the rest of your life?

1111 M: Well I'd had it two or three times before that, quite regularly. [okay] Sort of every three
1112 months.

1113 M: Ah because I didn't. she didn't erm - she didn't say oh we're going to watch, you know,
1114 you're likely to be on a pill for the rest of your life, although a friend of mine is, exactly
1115 the same as you, erm but I never asked him the questions, that's why I'm interested of
1116 why they came to that decision because mine - mine didn't. when I went back for that,
1117 the second time, she didn't say well, it looks like we're going to have a look at this and
1118 put you on a long term pill.

1119 PC: She didn't say that?

1120 M: No. because I'd - I'd read up on that one, and she was a little bit - obviously they cost
1121 more money, I don't know, she was a little bit erm oh well, I suppose so, sort of thing, so
1122 I said go onto this and have a look at it yourself and she read it, that's the baby, and it
1123 sure is.

1124 M: Well I've had about four very severe attacks in - in a two year period. [ah right] And
1125 when I had the last attack the GP said well, we'd better come in and [yeah] consider
1126 what treatment we should give you.

1127 M: Because you obviously...

1128 M: But the thing he asked me was is it affecting the quality of your life and I said when you
1129 get a period of like six weeks...

1130 M: Re-attacks.

1131 M: ...erm ten days of really severe pain and then sort of petering off...

1132 M: Then coming back again.

1133 M: He said it's obviously affecting the quality of your life, so he put me on Allopurinol. [ah] I
1134 wish he'd done it two years ago.

1135 M: Right, so you're the same in that way, you had re-attacks? And you did?

1136 M: Yeah, yeah. Two or three.

1137 M: I'm just wondering how he came to the - to the I've got to have a pill.

1138 PC: At what point they...

1139 M: What about you?

1140 M: Well...

1141 M: Are you on the pill?

1142 M: ...I had a - the first attack I had I remember very well, it was very severe, big swelling,
1143 [yeah, yeah] big erm rash and the doctor looked at it and said gout, and I started the
1144 treatment there, there and then.

1145 M: Yeah but how did you come to have to stay on them, because I don't. I'm just worried
1146 that...

1147 PC: Yeah I would - yeah, there's - so apart from David, everyone is on long term every day
1148 treatment?

1149 M: Are you?

1150 M: Yes, yeah. 400mg a day.

1151 M: I'm on 100mg.

1152 M: I'm on 300mg of the sulfinpyrosan.

1153 M: All the same, all the same pill?

1154 PC: No.

1155 M: Allopurinol.

1156 PC: No, no, they're not.

1157 M: No because I got a reaction from the Allopurinol, so I got this other one.

1158 PC: There is a way of doing that and again I'll - once we've finished we'll talk about that, so I
1159 wouldn't worry too much.

1160 M: It's just interesting that, yeah.

1161 M: So I take two of those a day. And coltrasine as required. [right, yes] And like you take
1162 that as required don't you?

1163 M: Yes. Well I haven't got any more but I'll have to get some more.

1164 M: So you still get attacks even though you're on...?

1165 M: Yes, I get an attack about once every three months, four times a year roughly.

1166 PC: What do you think of that then, whilst all of you are on tablets, perhaps not for you
1167 David, [mild] but - and you're still getting attacks, what do you feel about that?

1168 M: [sighs] Well I'm sad about it.

1169 M: I tell you what, I don't know about you, but I find that if I see a - like my wife will have a
1170 cake, say a cream donut or something like that, and I fancy one, a cream donut, you
1171 know, and I'll say oh, I'll have one, within five days I'll have an attack of gout. [gosh]
1172 [wow!] Yes.

1173 M: Well I'm surprised it's five days, it's normally two.

1174 M: That's awesome.

1175 PC: So are you - so are saying your treatment doesn't work?

1176 M: Yes. [right] The treatment works, but I know that if I take dairy, dairy products...

1177 M: Bloody hell, just even one donut?

1178 M: But you forget the pain, that's the point, you've forgotten it haven't you?

1179 M: Yes. Because your body doesn't remember the pain does it?

1180 M: No.

1181 M: You can, you know it's erm...

1182 M: And as soon as you get it you think Christ, what an idiot I was [yes] to take that [exactly]
1183 maybe...

1184 PC: So beyond treatment, it's - you're saying it's more dietary and lifestyle than...

1185 M: Well the Allopurinol - Allopurinol works. I have had - I don't know if it's - because you'll
1186 perhaps go out and somebody is putting erm cream in the mashed potatoes or
1187 something like that, you know...

1188 M: Does that do it?

1189 M: Yeah.

1190 M: Bloody hell.

1191 M: Gosh, you've got it severe haven't you?

1192 M: Yeah.

1193 M: I'm worried now that I'm on top of the world, that it's [68:35] me. I might have another
1194 attack in...

1195 PC: It's interesting how people with gout listen to each other as well.

1196 M: Yes we're all different aren't we? We're all different.

1197 M: Can anybody else link, like dairy products? Because I sort of linked a few things to me,
1198 and as far as...so what about you, do you...?

1199 M: Well I'm still eating mussels and king prawns and everything like that.

1200 M: The Allopurinol I suppose is to let you do that isn't it?

1201 M: Yeah, [yeah] the thing that seemed to cause me a problem was if I stressed the joint in
1202 any way, [right] if it was...

1203 M: Because mussels are worse, and sardines, oily fish, but not so much king prawns, as far
1204 as I can see, because I bloody love them, and I...

1205 M: I like mackerel and all those things.

1206 M: I eat a lot of seafood, except oysters, I've gone off oysters now.

1207 M: I've never seen the point of eating oysters to be honest with you. [laughs]

1208 PC: Do you - it's interesting listening to all of your sort of different you know what sets it off,
1209 is there a like a group or someone you can talk to about you know like this, is there a - or
1210 would you like there to be a sort of...

1211 M: Never thought about it much.

1212 M: No, I've never thought about it.

1213 M: No, well I've found this very interesting to listen to what everybody is talking about, it's
1214 really interesting, because it's in the back of your mind all the time if it comes back
1215 again, knowing what the pain is like.

1216 M: What [69:49].

1217 M: And you think that's the last thing on this earth that I ever want to happen again. And if I
1218 have to do something a bit more drastic, I'd probably do it. But as things are, touch
1219 wood, erm I only had a very light re-attack and I can't really pinpoint anything I was on
1220 holiday, so you tend to over excess, so going back to your moderation thing, I guess
1221 [yeah] it's like all aspects of life isn't it, if you - I probably drink too much but then erm
1222 the red wine hopefully doesn't do anything but...

1223 M: I'm interested that you've tied it to drink because...

1224 M: No, I did - no, that was a contributory factor and two other people in the club who were
1225 on the same beer at the same time, [yeah] erm both got gout.

1226 M: Because this is the old thing, from oh the middle ages, that it's due to drink.

1227 M: Well of course but I had a lot of - I don't normally drink port at all, erm I wouldn't say -
1228 we have the odd glass at Christmas, with a bit of cheese, but this was a one night, in
1229 amongst the same period [yeah] when we'd had a big dining out job and there was a
1230 cheese board and I think just over excessed on the...

1231 M: The cheese...

1232 M: Until I went on the NHS site I'd never linked beer with gout.

1233 M: Well I didn't, but it does...

1234 M: Erm port and red meat.

1235 M: But then...

1236 M: That's alcohol isn't it? Any alcohol?

1237 M: When you look at the yeasty thing, and I thought marmite, yeast extract, erm...

1238 M: You're a marmite fan aren't you?

1239 M: I love marmite, I love it. But I've never associated it with attack.

1240 M: It does, honestly, yes it's a high contributory factor. Because of the yeast. And the Coors
1241 Lite I was thinking it's American...

1242 M: Because you know what they make it out of don't you? It's yeast from the brewery.

1243 M: Brewer's yeast.

1244 M: From the brew.

1245 M: You know the brewer, the brewery, [yeah] it comes from there and it goes up to
1246 marmite and they make it...

1247 M: If you drive through Burton on Trent you get - you get...

1248 M: I didn't come here to get put off marmite. [laughs]

1249 M: Cut it down, cut it down. Cut it down.

1250 PC: Well you do what works for you Richard, that's it, you know.

1251 M: Yeah exactly. This is what I'm trying to say, everybody's erm...

1252 M: I'm telling you.

1253 M: ...erm what's the word?

1254 M: It's distinctly mentioned that marmite, by name.

1255 M: ...metabolism is different, everybody is different.

1256 M: But you drive through Burton on Trent, you've got - you've got the Coors Brewery
1257 coming out of one nostril, and the marmite factory coming out of the other and you get
1258 more yeast at the end of the brew than you start with, and you're driving down the road
1259 to the marmite factory, aren't they? [yeah] It's true.

1260 M: Yeah, yeah. Well all I can do is reiterate that in the 42 years I've had this, I have only put
1261 it down to two foods, three, that give it to me, grapefruit, kidney and liver. [okay]
1262 everything else is - it's a bit...

1263 M: He'd never thought about marmite. [laughs]

1264 M: Seriously [72:21].

1265 PC: Right, we're just going to try and...

1266 M: Cut - halve it, just halve it. [laughs]

1267 M: No, [72:30].

1268 PC: We're trying to - we'll try and wrap up now gentlemen, [okay] because erm I realise
1269 you've been here for a while now, so anything else that you think is important about the
1270 treatment of gout, or how it can be improved in the future, any sort of thoughts, final
1271 thoughts on that?

1272 M: Well if you're going to do a - if this all - all this is going to do with your erm experiment
1273 [research] [yeah] research, hopefully something will come of it, that you'll be say a little
1274 tiny 1mg pill can replace all of the thousands of milligrams we have to take [73:05].

1275 M: They could put something in the beer.

1276 M: Yes.

1277 M: Well you need yeast, otherwise you won't get beer, you know, alcohol.

1278 M: All right, in the wine. In...

1279 M: Wine's all right for some reason.

1280 M: No I'm just saying, you know, the erm...

1281 PC: So you just think there should just be one tablet that does the job?

1282 M: Well obviously as research goes on, [yeah] obviously I mean to take loads of pills every
1283 day, whereas reduce it down to one little tiny pill once a month.

1284 PC: Okay, that's interesting.

1285 M: I would say in doctor's surgeries and that, because as we get older we do tend to go
1286 more, if there was in the leaflet cabinets, the erm - if they had one for gout as a sort of
1287 this might help you, don't eat bloody marmite...

1288 M: Don't drink that beer that you said, [laughs].

1289 M: Yeah, yeah. And things like that, and it said well these are helpful hints [yeah] that may
1290 prevent you getting gout, and don't have too much of this or too much of that, and you
1291 could - I mean that's self regulatory is the key and moderation. So we all overdo things.
1292 [right] I think that would help.

1293 M: I think modern surgeries these days, they do a blood test for cholesterol, [yeah] why
1294 don't they extend it to...

1295 M: Yes, good one, good one.

1296 M: ...to actually monitoring your uric acid, and saying to you look...

1297 M: Well yes, I think they should do that.

1298 PC: What you mean...

1299 M: It's up to your GP, all he's got to do is put a uric acid...

1300 M: Tick the box.

1301 M: Yeah, tick the box and say to you look, you've got a high uric acid, you've a possibility to
1302 [okay] have gout. And in my case I think I've had low level gout for ages.

1303 M: That's a good one actually because you can tick the box.

1304 PC: So you think it should - even before you're diagnosed someone should check it and warn
1305 you [yeah]...

1306 M: As part of the blood test.

1307 M: Warn you that you have...

1308 M: [74:38]

1309 M: ...and you know like with cholesterol say [okay] well if you take this pill, there's a
1310 possibility...

1311 PC: Okay, that's interesting.

1312 M: What does everybody eat from all cultures and everything, it's bread. So what you want,
1313 you want you - you egg heads here want to come up...you want to come up with a drug
1314 that you put in bread...

1315 M: An additive. [right]

1316 M: That nobody - well you've got to - they've got to know they take it of course, in most
1317 countries they've got to know, that prevents gout.

1318 M: Morrison's have the [okay] - the anti-gout bread.

1319 M: Or [75:14].

1320 M: I'd prefer it to be put in red wine. [laughs]

1321 PC: Nick, any final thoughts from you?

1322 M: No, I think we've more or less said erm most of the things that we're about.

1323 PC: Okay, great. Okay, anyone else, anything before we...?

1324 M: Well that question to you, can you have low level gout? Is...

1325 PC: Yeah you can, so gout doesn't have to be an acutely painful red hot toe, you can have
1326 gout in between those typical attacks and you can have pain in the joint in between
1327 those really, you know, red hot throbbing joint pains. So erm you can do, yeah,
1328 absolutely.

1329 M: And you can have it without having the really severe attacks as well. Can you?

1330 PC: Yeah, yeah. So it's - it's interesting that, you know, some of you mentioned that it's
1331 chronic pain that is associated with gout, not just during that attack, so whilst you think
1332 well, there's no gout there now, it doesn't look red hot, swollen, you might still have
1333 pain.

1334 M: Yeah that's what I've - yeah.

1335 PC: Yeah, that's totally acceptable.

1336 M: I've got something to add. Erm my daughter had a canary with gout. [right] [what?] A
1337 canary.

1338 M: How did they diagnose that?

1339 M: The vet.

1340 M: What, took a blood sample and there's too high a uric acid?

1341 M: Yeah and I mean it would go wild if you tried to catch him, but if you caught hold of him
1342 like that and just rubbed his legs, he'd got it in his knee joints, you rubbed his legs and
1343 he was quite calm.

1344 PC: Right, not heard that one before. There you go.

1345 M: Well, there's a thing.

1346 M: I - my experience would be it should be publicised more that you know these sort of
1347 aches and pains [right] that you think you're getting as you go into old age, it might
1348 actually be linked [mmm] with high uric acid. Have it checked.

1349 PC: So you think people need to be more aware of it?

1350 M: Yeah more aware of it. Yeah. I think there may be lots of people, you know, as I say I
1351 played sport all my life and people as they get older they say oh I've got these aches and
1352 pains in joints...

1353 M: Well like blood tests, like you said. That would do it.

1354 M: And a straightforward blood test telling you, hey, [okay] be careful, you've got a high
1355 uric acid content. [mmm]

1356 M: And sorry, just one last question, [yeah] a medical question, these crystals in your joints,
1357 [yeah] they can cause permanent damage can't they?

1358 PC: They can indeed.

1359 M: Then it comes out as osteoarthritis.

1360 PC: And actually it's interesting that it hasn't come out yet in the discussion, that the whole
1361 aim of treatment, or long term treatment, is to prevent this permanent damage in the
1362 [yeah] bones because the bones get eroded or eaten up by this continuous
1363 inflammation [friction] with gout, so [yeah] what you're trying to do with long term
1364 treatment, is to prevent this irreversible bone damage, [yeah] so the treatment is very
1365 much erm - sorry, the damage is very much permanent if you don't get on top of it.

1366 M: Is that in the ball joints and things?

1367 M: Any joint.

1368 PC: Yeah, any joint.

1369 M: Any joint, you can get it in any joint. I'm surprised he's had it in his chin. I've never heard
1370 of that before.

1371 M: You've never seen...

1372 M: But I've had it in my arm and my knee.

1373 M: Doesn't it disperse, the crystals and that?

1374 M: The last time I had it was in the knee.

1375 M: [78:19]

1376 PC: Yeah so it basically what happens - we'll just erm...finish and then we'll talk about this
1377 because I think it's probably not relevant to our overall discussion, but erm is everyone
1378 happy with...with...

1379 [general agreement]

1380 F: Can I say something? [yeah] [laughs] My dad had treatment for a heart condition, they
1381 changed his heart pill, he got gout, he went back to the doctor, the doctor changed the
1382 heart pill and the gout went. And there was never [oh] any proof, but the doctor
1383 straightaway looked at the tablet and said it's that one, right, okay. And he never had it
1384 again.

1385 M: Which was it?

1386 PC: It's - it's erm...so certain tablets which you take for blood pressure or heart conditions,
1387 erm particularly the diuretic ones, are well known to predispose you to gout because of
1388 the way [oh] they act on the kidneys. And it's the whole [yeah] idea is you know related
1389 to the mechanism of you getting uric acid out.

1390 M: I'm on remapril I am.

1391 M: Yeah, I have remapril.

1392 PC: So if they have an affect on the kidney which disturbs that mechanism of getting the uric
1393 acid out, you are more likely to get gout.

1394 M: I'm on four heart pills at the moment.

1395 PC: I'm just going to switch these off gentlemen because we don't want any personal
1396 medications or details on this.

1397 M: [79:30]

1 **Focus group transcript 2**

2

3 PC: = MODERATOR

4 M: = MALE PARTICIPANT

5 F: = FEMALE PARTICIPANT

6

7 PC: Right, ladies, lady and gentlemen. So erm I just wanted you to sort of talk to me and
8 each other really about what your experience has been with the treatment of gout and
9 how you feel it's had an impact on your life and the quality of your life overall. So feel
10 free to start, whoever, and you can use your own experiences, you know, when you
11 were diagnosed and whatever you want to say really, there's nothing that you can't say.
12 Okay, go on Margaret.

13 F: What do you want me to...?

14 PC: The gentlemen want you to start, so...

15 F: Well I've had gout for about five or six years. [okay] And when you do have it, it's just
16 agony. [yeah] But the worst of mine if my feet and my fingers, my fingers are terrible.
17 [okay] I'm in agony with these joints. [yeah] But those are the tablets he's put me on,
18 the hospital. [okay] So...

19 M: I'm on the same.

20 PC: You're on the same?

21 F: Are you on these?

22 M: Yes, I take one every night.

23 F: I have one in a morning. Yeah. I've been on these two or three years now.

24 PC: Have you, and what do you think about those tablets?

25 F: I think they're good. [right] Yeah.

26 PC: Same for you, Les?

27 M: [1:11] no problem since I've been on them. I've been on them for 20, nearly 30 years
28 now. [okay]

29 F: Have you? 30 years?

30 M: Just taking one, one a night, it keeps it...

31 F: Yeah see I had to go in hospital because all my fingers were up here and all this [yeah]
32 [right] was terrible, I was in agony. [right] And in my toes.

33 PC: Okay, and what about you John, are you on any...?

34 M: I don't have any treatment at all.

35 PC: You don't have any, and why is that?

36 M: I have occasional flare ups and I have ibuprofen for three or four days, [right] and it
37 disappears quite easily.

38 F: And where does it hurt you?

39 M: Pardon?

40 F: Where do you get the pain?

41 M: Erm mainly in my big toe, the classical sort of place, [yeah] but I do have it in this thumb
42 here now, but that's it.

43 PC: Right.

44 M: And I literally have very few problems from it, that's - it's two sort of thing, and it's
45 usually a traumatic sort of thing, I've either hit my toe or hit my thumb of done
46 something [yeah], and it seems to be trauma related.

47 F: And them tablets take it off do they?

48 M: Uh uh, the ibuprofen does it and takes it down. That's it.

49 M: I...

50 M: This is Allopurinol that you're taking?

51 F: Yeah, yeah. Allopurinol.

52 M: [2:17] terrible but erm I was in the licensed trade as well, that made it really awkward.
53 But erm I was fortunate that A, I couldn't drive my car, because it - my left foot, and erm
54 - but I was fortunate that a friend of mine had an automatic car, and we used to swap
55 cars, so I'd drive his [ah] [right] with one foot.

56 PC: So you had to sort of adapt [yeah] because of that, and this is before you went on the
57 treatment is it?

58 M: Oh yeah, yeah.

59 PC: Right, okay. Okay. So are you quite happy with the way things are then, because how
60 many attacks do you...?

61 M: I'm absolutely happy with it, erm yeah, [gout] I suppose I'm a bit of a fraud here really I
62 think really, it's [laughs] oh, it's...perhaps once or twice a year.

63 PC: Right, right. [or less] And your doctor's haven't recommended going on a long term
64 treatment?

65 M: No, no.

66 PC: Is that something you would consider?

67 M: Well if it got worse, yes I would but certainly at the moment I don't need to bother
68 about it really, it's a very, very - no worse, in fact I would put it down to aches and pains
69 getting aged really rather than anything. [right] I mean we know it's a specific sort of
70 thing, it is - you know, the pain is excruciating, when you've got it in your big toe. You
71 can feel the blanket in the bed, it seems to hit on it, but yeah, it's you know a classical
72 sort of thing. [yeah] [yeah]

73 F: But I find it's difficult undoing bottles anything to undo. [yeah] I live on my own and I
74 have to go out on the front, somebody passing, but I live - my brother lives by me so he
75 helps me with - when we go shopping, [yeah] will you open this for me before you go?
76 And I brought this and that's good.

77 PC: Oh yeah.

78 F: That's [ah] I had that from a charity shop. [right, okay] It's good that it. Yeah.

79 PC: Okay.

80 F: It helps me.

81 PC: Yeah good. And so when you were all diagnosed with gout did you - were you aware of
82 what sort of treatments are out there, or what's available?

83 F: Well...

84 M: I knew what treatments were available. Erm...

85 PC: And how was that? Is that something you've read up or friends or family?

86 M: I'm sort of in your business, type of thing.

87 PC: Oh right, what do you do?

88 M: I was Director of Pitfield Research, cancer research at the hospital.

89 PC: Right, okay, okay.

90 M: So it did sort of come down into these things as well.

91 PC: Right, [yeah] and what about you, both of you, did you know what treatments were
92 available and...?

93 F: Well no, it was all my hands swelling up, fingers and that, they didn't keep me in but I
94 went in the ward for a few hours, and they were talking [right] to me about it, and he
95 says have you ever heard of Allopurinol? [right] He says that's good for gout, the doctor
96 said, I said no, I haven't. [okay] So he put me on them.

97 PC: Okay, right.

98 F: So I can't really grumble because they are good.

99 PC: And do you take anything else when you get an acute sort of attack or is that the only
100 thing that you take? [no]

101 M: I only have the odd flare up, just about - as the gentleman said, lasts a couple of days
102 and not - not bad. Just little twinges. And - but erm it goes off pretty quick. [yeah] [right]

103 F: Yeah, it does go off pretty quick. But [yeah] I can be walking, doing my shopping, and all
104 of a sudden, I'm in agony, [yeah] I can't walk to the till. Oh my god, you know, you're
105 glad to get home. It's a terrible feeling. [okay] And it can last five days with me. [yeah]
106 Now at the moment it's pretty good, all of it. [okay] But it can come on...and you don't
107 know.

108 PC: Out of the blue?

109 F: Out of the blue. Yeah. [right]

110 M: I never get that, I usually know it's - it's a gradual sort of thing, and I think that's it, I've
111 usually taken the - or I start taking the ibuprofen I know what that is, [yeah] and then
112 you know - and it drifts off. Occasionally it does sort of catch me unawares, [yeah] but
113 not very often. Do you find hydration affects it, if you don't drink?

114 F: Drink?

115 M: Erm...

116 M: I don't mean alcohol, drink you know water or something.

117 F: Oh I'll drink water.

118 M: If you haven't drunk water for a bit do you find that you get it more?

119 M: I've never really noticed that. No. [oh]

120 PC: Yeah different people find different things does bring it on.

121 M: I sort of find if I'm dehydrated, it tends to be, you know, more than if I'm not. [yeah]

122 M: Yeah that's a point, yeah.

123 F: I drink plenty of water.

124 PC: Do you? Good, good. So overall would you say you're all quite satisfied with your
125 treatments at the moment [yeah] for gout? Yeah?

126 F: Not unless there's anything else come out, I don't know. You know.

127 PC: Right, would you want anything else if that's working though?

128 F: Oh no, no.

129 PC: You're quite happy with that?

130 F: Oh no, now and again I take a paracetamol [okay], now and again. You know.

131 PC: Okay, so is there anything you want to treatment, you know, for you to improve or
132 achieve something else?

133 F: I don't know really.

134 PC: For example, how do you feel that you still get flares, even though not for you John, but
135 for Les and Margaret, if you're on long term treatment and you're still getting flares,
136 [yeah] does that - how does - how do you feel about that?

137 F: Well, yeah, yeah.

138 M: Well [7:15] I get about twice a year, so [7:21]

139 PC: So you don't mind?

140 M: I'm not really bothered.

141 PC: Right, right.

142 F: Oh I can have it more than that.

143 M: Do you relate yours to an injury? [pardon] Have you banged it or kicked it or hit it or
144 banged it or something?

145 M: Erm I broke my ankle once, [7:36] erm but not probably...

146 M: Because it may sound daft but the first time I had mine diagnosed I hit my toe with a
147 squash racquet, and I thought oh, that's hurt me...

148 F: It'll go off.

149 M: It'll go off. But it didn't and then erm Gordon Thomas here sort of said you've got gout,
150 and that was it. And that's ten years ago I should think.

151 PC: Right.

152 M: But that was the first time and then since then it's been little odd knocks and injuries.

153 PC: So whichever joint you knock or injure, that sort of gets gout does it?

154 M: Well one was put down as housemaids knee, that's kneeling on a hard - sort of a hard
155 surface, but erm I don't think it was, I think it was probably gout. I don't know, but it
156 probably was and it went off with the ibuprofen just the same. [yeah] [right, okay] As I
157 say, this joint here, I can hold glasses in that hand but [yeah] I can't hold glasses in that
158 hand. [8:21]

159 PC: And has the treatment had any effect on any other aspect of your life, obviously you
160 know it controls your gout attacks, what about other things, you know, impact on your
161 work life, friends, family, anything like that?

162 F: No.

163 M: Erm I suppose well it used to affect me with me being in the licensed trade, it erm - it
164 erm - you sort of adapt, you have to. [yeah] But then I wasn't on those.

165 F: They are good them are. [okay]

166 M: But Dr. Thomas put me on those...

167 F: By my brother - my brother has gout terrible, he should be here really. [right] He has it
168 terrible and he's a lollipop man, he used to be a teacher's lollipop man now and he has
169 to go work in his slippers, whatever the weather. [mmm] Can't walk. [right] He's in
170 agony.

171 PC: Okay, okay.

172 F: And the stuff they gave him to take for it affects his stomach. [right]

173 M: Oh yeah, yeah.

174 F: So he's been back to the doctors, and he's give him something else and the stomach's
175 gone better now and the gouts going off now.

176 PC: Okay and none of you have had problems with side effects from your medication?

177 M: Oh no, no.

178 F: No, no.

179 PC: No, okay.

180 F: I find it not very good getting upstairs but you have to try your best.

181 PC: Yeah and do you know why you're on long term treatment? What's, you know...[no] has
182 anyone explained to you what the sort of rationale is for taking these?

183 F: It says don't - don't...

184 M: Years ago but I can't remember now.

185 PC: Can't remember.

186 F: Your doctor will tell you to stop taking these. That's it, just after food with a glass of
187 water, you have to take plenty of water with these. [yeah] But erm the doctor will tell
188 you when to stop.

189 PC: When to stop, so you just...

190 F: But he hasn't.

191 PC: Yeah, yeah. But did they tell you why they started it in the first place?

192 F: Well because of all this pain in my fingers, [yeah] and hand. The hospital put me on
193 them.

194 M: It wasn't erm...it's just erm you know...[10:20] it doesn't cure, it just helps, helps to
195 [yeah] keep it at bay. [yeah]

196 F: Yeah, it doesn't cure it. Because it wouldn't come back again if it cured it.

197 PC: That's right. Yeah. Yeah.

198 M: Oh no, no. but I've really had no trouble really since I've been on them. [okay]

199 F: How long have you been on these?

200 M: Oh 20 odd, nearly 30 years.

201 F: Always had...mmm...

202 M: You know all the...

203 PC: Right, and apart from tablets, have you had any ideas, has anyone told you that there
204 are the treatments for gout? Are you aware of any of the...[no] not really?

205 F: No, they haven't.

206 M: Sort of all right on those so he just carried on with those. [yeah, no]

207 M: I feel contented with what I'm - what I'm doing really and some of the others probably
208 have worse side effects than the actual gout itself, so I think it's a - it's a catch 22
209 situation really. [okay] [yeah]

210 PC: Yeah, yeah. Right, okay. Erm...if you sort of met someone else who had gout, is there
211 any sort of what sort of recommendations would you suggest or is there anything you
212 would tell them specifically about...?

213 M: I think I'm a bad example of this really because I don't think, you know, it's...

214 PC: You don't think it's...

215 M: It's not you know, I mean people say they've had gout and I mean that's a huge, great
216 spectrum. But I mean one of the lucky ones I suppose, [oh yeah] you know that doesn't
217 bother me. I think it depends how seriously you have it, [yeah] if it's crippling or
218 something then - or which joint you've got it in, or where you've got it. [right] I mean a
219 toe is relatively innocuous, if you've got it in your knees or hips or something, then yeah,
220 it's a little more worrying. [yeah] If it was disabling, then you'd...

221 PC: Okay, so for you it's not disabling?

222 M: It's not disabling at all, no.

223 F: Well how did they get you to come here, the doctor or your doctor or...?

224 M: As I say the first one was erm ten or 11 years ago when I hit my toe and that was why it
225 started and he suggested try the ibuprofen and it was off in two or three days. And so I
226 tend to keep a little stock, it sounds wrong, but a few tablets [yeah] and then start it and
227 erm it's usually three days, 600mg three times a day. And [yeah] it's gone. So it is a bit of
228 a - you know I think I'm a fraud in a gout study really,

229 PC: Do you think? No, we don't think so at all because that's the exact reason we wanted to
230 sort of look at the range of you know, how people are affected so as you said some

231 people may not be affected that much, whereas others have it really quite severe, so it's
232 interesting to...

233 F: It's very, very, very painful.

234 PC: Yeah and...

235 M: Yeah I agree with that, yeah.

236 F: It's [12:56] really.

237 PC: Yeah, yeah. And that pain, does that...

238 F: And it does make you cry.

239 PC: Does it? Mmm.

240 F: Yeah if it's bad, when it comes on. Really bad.

241 PC: And I was going to say, does that affect you in any other way, obviously the pain can
242 have affect on other aspects of your life, has it sort of caused any I was going to say
243 problems, but has it had any impact on any other areas of your life at all?

244 M: No.

245 F: Not really, no, you just try your best and you know it will go off.

246 PC: Okay, so the pain does...

247 F: See, you don't know when it's going to affect you. [yeah] Come on this afternoon or
248 three or four weeks.

249 M: It affected me in as much I worked behind the bar, so [yeah] when I got an attack it was
250 painful and [yeah] erm one time I kept a sports club at Stoke, erm one of the committee
251 men used to take over the bar and I used to take over the committee job, [laughs] [right]
252 swapping and changing like, we got round it like that. [yeah] And as I said because that
253 was quite easy.

254 M: I played a lot of sport and a lot running, and once it would stop me doing that because it
255 was just painful to bend your toe. [oh yeah] You couldn't do it, but it was less than a
256 week and I think three days is probably the maximum amount it sort of [okay] you know
257 made me sore.

258 PC: Okay, [yeah] and do you do anything to prevent it coming on? Are there anything you
259 can do...

260 F: Well you don't know when it's going to come on.

261 PC: So you can't do anything?

262 M: Well they say certain foods can cause it don't they?

263 F: Well they used to say rich living caused gout. Rich living caused gout.

264 PC: Absolutely, yeah. Is that still the sort of common understanding, like your friends and
265 family, do they think...

266 F: No, oh I do eat well. But not that well.

267 M: Yeah, it's a joke. Well it's a standard thing for the government now isn't it, they think
268 they're curing us all really by making us not live so well. [laughs]

269 PC: Fair point. Erm yeah, no, it's interesting actually because as you said, I've come across
270 that before as well, that it's a disease of the kings and...

271 F: Yeah, rich living.

272 PC: ...and yeah, rich living. And erm...

273 F: Eating well [yeah] can bring it on.

274 M: I think a lot of people [15:17] on their liver, liver and onions and...

275 PC: That brings it on does it?

276 M: Yeah but I'm afraid I like it occasionally. [laughs]

277 M: I do. Yes, I do.

278 F: [15:22]

279 M: Yeah, no, I can't notice any sort of dietary sort of...

280 PC: No, you don't change your diet or...

281 M: Not really, no.

282 M: No.

283 PC: No, so have you had any information about sort of diet and what you should and
284 shouldn't do?

285 M: No.

286 F: No.

287 M: No.

288 PC: Right.

289 F: No, nothing.

290 PC: Something - is that something you'd be interested in, something you'd probably like
291 from...you know doctors or...?

292 F: Yeah I wouldn't mind if it can bring it on eating certain food. If it would help, you know.

293 PC: Right, okay, okay. Erm and how do you think we can sort of improve the management of
294 gout overall in the future, any thoughts on that?

295 F: What's brought this up, this about gout?

296 PC: You mean this study? [yeah] Well it's just really common to, you know, it's affecting
297 about 1.5% to 2% of the population, which is quite common, it's more common than
298 rheumatoid for example, [rheumatoid arthritis] erm and it's - and particularly in the
299 community, so most people are treated and you know by their GPs, but there haven't
300 been any studies about how people present what they want out of the treatment, erm...

301 M: Doesn't this say something of the long term sort of policy, I mean one time I suppose if
302 you came along to a path lab you got your uric acid measured only if you had a specific
303 gout thing, but now it's part of the sort of screening that comes on. So it's probably
304 something that's found in it's a long term screening look at your creatin, look at your -
305 your things [yeah], it's part of the screening, I mean a lot of people have treated on
306 results really now, to bring them back in the algorithm you know of normality. Blood
307 pressure, erm cholesterol, also you get your erm [yeah] your aspirins, your whatever
308 they call it, erm...statins, which people would have been outside of the limit, but now
309 you're treated to bring yourself down into the norm. and you know are people being
310 treated for oh look, your uric acid's a bit high, so we'll treat his gout now. It was
311 probably not [17:18].

312 PC: Do you think they are, they are being treated like that?

313 M: Yeah I do, I do. I think a lot of people are. [right] And they're - they're...

314 PC: Okay, so even though they haven't got the symptoms, the blood test is high and then
315 you get a tablet, is that what you mean?

316 M: Yeah I think it is probably. Yeah. [okay] We'll treat the uric acid and not the symptom.
317 [right] They may get it later on. [yeah] They may be right.

318 PC: Yeah, yeah. And what point do you think people should go on treatment, or long term
319 treatment, for example if you're having - you know, how many attacks would you say
320 should be treated, you know, in a year should be treated?

321 M: I think, yeah, yeah, well I mean when you've got it, you want it treated, you want
322 something done about it, [yeah] you do want it done. And I find mine just goes quickly,
323 so I'm tremendously happy, I wouldn't want to be on long term Allopurinol, not because
324 there's anything wrong with it, or anything, or anything else, I'm very, very content with
325 what I've got. But I'm sure that, you know, if I hadn't had the pain in my toe, and I had
326 not found if uric acid was raised, and I probably wouldn't have been treated.

327 PC: Okay, right. And why would you not want to be on Allopurinol, is there any specific
328 reason?

329 M: Well there's - the clearance is okay, [18:28] all right, runs along, then I'm quite happy
330 with it. But I think all you're doing is increasing the clearance of uric acid a little bit, it's
331 erm - it's - I would rather just drink a lot of water I think really, which probably might
332 have the same effect. [right] Or, as you say, stay away from rhubarb I think at one time
333 wasn't there, I eat rhubarb twice or thrice a year, so it's not really you know, a rhubarb
334 diet.

335 F: Rhubarb? Mmm.

336 PC: Okay.

337 F: I don't eat rhubarb.

338 PC: No. and...

339 F: Not unless I have a rhubarb yoghurt. [laughs] A yoghurt with rhubarb in.

340 PC: Yeah. Erm and both of you don't have any sort of reservations or any problems about
341 being on treatment with the Allopurinol?

342 M: Not really.

343 PC: Not really? No.

344 F: No, not unless they do bring something else out and we don't know, I mean...

345 PC: Yeah I mean there are other treatments but they're fairly similar to the Allopurinol and
346 erm you know you don't need to go onto them unless you've had a problem with the
347 Allopurinol, that seems to be the standard treatment really. Yeah. Yeah. Okay. Okay.
348 Erm so yeah, so coming back to the question of how to improve things in the future,
349 what would you like being done about it, from your point of view?

350 F: Well if they come something else out, and your doctor's sent for you and put you on it
351 and try it, you know. [okay] I don't know really.

352 M: Me, I don't get any trouble now with it, so I'm happy as things are and I can't really say
353 people with really troubled with gout, obviously they need different tablets to combat
354 it, but erm...I'm same as John, I - I'm quite happy with what I've got because [yeah]
355 we're not really bothered by it.

356 PC: Okay, and the medications, has it had any sort of impact on you know your other
357 medical conditions, or you know financially or anything like that, has it made any
358 difference to your erm sort of life in any other way at all?

359 F: Erm...I don't think so.

360 PC: Because a lot of the time people who have gout may have other problems, [oh yeah]
361 and then the treatment gets very tricky...

362 F: I've got other problems.

363 PC: ...because the tablets may interact.

364 M: [20:54]

365 F: Yeah but I think your doctor sees about that. [yeah] Because when I have something else
366 new I say am I all right taking these with what I'm on.

367 PC: Yeah, so you check, right. Okay. Okay.

368 F: And they seem to have - it doesn't affect me, [okay] somehow, you know.

369 PC: No, and are you aware of sort of the difference between the treatment of acute gout
370 and sort of when you know it's not flaring up, because there is a difference.

371 F: Oh yeah, you feel better don't you in yourself, [right] if you aren't in pain.

372 M: Well I'm - I come under that category because I'm all right now more or less, [right,
373 okay] whereas I used to suffer with it quite a lot.

374 F: But yours could flare up again at any time.

375 M: Oh yeah.

376 F: Can't it?

377 M: Oh yeah, yeah. You get the odd twinge and that, yeah.

378 F: Yeah you don't know when it's going to come. [no, no] But you know you've got it.
379 [yeah]

380 M: I'd agree with that.

381 PC: Have you ever come off your treatments?

382 F: No.

383 M: Oh no. [no] I've stayed...

384 F: I always take these first thing after my breakfast. [yeah] One a day.

385 PC: So would you - like now that you're fine and you don't get flares, would you consider
386 stopping it?

387 F: Oh I don't know.

388 M: I don't know. [laughs] I'd rather stay as I am I think.

389 PC: Right. Okay. [yeah] Okay, and did you know much about gout before you were
390 diagnosed, through other sources, like - for you John it's probably different, because
391 you've been in the business, but...

392 F: No, not really, no.

393 M: You heard of it.

394 F: You heard of it, but yeah...

395 M: Joked about it, but erm...

396 PC: You joked about it?

397 M: Well you did didn't you?

398 M: Yeah, you have to have one of those [22:29] things around your foot don't you really,
399 you must have one of those.

400 PC: Why do you joke about it?

401 M: Are you too young to have seen those? Oh dear...

402 PC: I have seen it actually. I have seen a photo of it. But erm...why do people joke about it?
403 It's a painful condition, you've all said.

404 M: Yeah, but it's...

405 F: Oh how!

406 M: It's historically a joke of the rich really isn't it?

407 M: Or drinking port or...

408 M: Yeah, port. Yeah. Oh you're having a wonderful time. Yes, I think it is a [yeah] - it's
409 historical isn't it really?

410 M: Yeah, good living.

411 M: I think probably kids in comics, they always have somebody [oh yeah] who was rich
412 always had a bad foot, you know, old king Cole and people have it don't they?

413 F: Yeah.

414 M: It retains that kind of erm - yeah I think there's certain diseases that are quite humorous
415 to - and they're not, but they're humorous to everybody else who hasn't got them.

416 M: Oh yeah.

417 PC: Yes, yes. And do you think that might be a reason, you know, people...

418 F: Well if you tell anybody, say what's - you're not walking very good or they say well
419 what's the matter with you? [yeah] I say well it's gout I've got. Well, rich living, see.

420 M: That's right.

421 F: Straightaway.

422 PC: How does that make you feel? Does that make you feel sort of, you know, like you can't
423 talk to people?

424 F: Well, I feel like hitting them. [laughs] [yes] You want to have the pain, well it...

425 PC: Yeah, yeah. Do you think that would affect people coming forward, like people
426 admitting that they've got gout maybe?

427 M: Erm...

428 F: I don't know.

429 M: I don't know, it's a joke I know I accept it.

430 M: Oh yeah.

431 PC: Yeah, okay, okay.

432 M: There's a lovely - you may have seen this, there's a lovely programme on television
433 which you should try and find on iPlayer or something, there's one of the Madam
434 Bouquet things, [oh yeah] Hyacinth one...

435 PC: Keeping Up Appearances.

436 M: Keeping Up Appearances. [yes] And it concerns gout and they have a better life because
437 he had gout rather than an ingrowing toenail. [laughs] It was much preferable to have
438 that because [24:14] so it's a little thing you could have a look at, [okay] you'll perhaps
439 see a little bit of the you know - the perception of gout.

440 PC: Yes, no, I have seen it but I've not come across that, so yeah, thank you.

441 M: Well it's in there somewhere along the line. But...

442 PC: Okay, right.

443 F: Yeah, I love that programme.

444 PC: Yeah, yeah. Yes, it's interesting actually how media sort of picked up on it as well
445 recently, there's been articles in the newspaper about gout, so yeah, yeah. [yeah] okay.
446 Good. Erm anything else that you want to add about sort of the diagnosis or the
447 treatment or erm...you know just sometimes people get quite frustrated because the
448 diagnosis maybe quite difficult and it takes months and years to actually diagnose it, has
449 that been a problem with you? Sort of...

450 M: Not if they have a full blood test, I think if they have a full screen, I think they are
451 [25:11].

452 PC: Yes, sometimes they don't get that though.

453 M: Don't they?

454 PC: No, because people just think well it's aged toe or...

455 M: I thought it just came on.

456 PC: Or you know it's arthritis, or whatever so...

457 M: You would think - wouldn't you think that more are diagnosed from their results than
458 actually from the seeing the patient?

459 PC: Erm...

460 M: In an elderly population.

461 PC: I'm not sure, I think it's - it has to be a combination of the clinical and the blood test
462 really, rather than just one or the other. Erm...because a lot of people, as you said, who
463 have high uric acid levels don't go on to get gout. So you can't really say you've got gout
464 just because you've got...

465 M: But then would you consider treating the higher uric acid rather than the gout?

466 PC: That's an interesting debate actually, erm and people have mixed feelings about that. I
467 don't know, what's your feeling on that, John?

468 M: I think if you've got uric acid you should look at your clearance really, either your
469 clearance rate's crap in the urea, that kind of thing, and certainly if you're knocking - you
470 know going under 40% clearances, then I think you treat it.

471 PC: Right, okay.

472 M: I mean you don't really get any serious effects until you get down to about 25%
473 probably, but by then it's probably too late. If you can retain somebody at 40%
474 clearance, you're not doing too bad. 25% you're running into problems.

475 PC: How do you mean it's too late, because you know you said that gout doesn't really do
476 much sort of long term damage to you...

477 M: It needn't be - it needn't be the - the gout is just a function of the clearance isn't it?
478 [yeah] And you're going to run into other troubles, I mean certainly if you've you know -
479 if it starts knocking off parts of your kidney, nephrons or something, then you're running
480 into serious problems. And that's probably an indicator that it is going down hill.

481 PC: So, all of you, Margaret and Les as well, do you associate gout with any other medical
482 problems or do you think like John said it may cause problems in other areas, if you
483 leave it untreated or...?

484 F: I don't know.

485 M: I suppose if you leave it untreated you could get problems, but...

486 F: Well you're in that much pain, if you didn't take anything for it, and you didn't know
487 what was the matter with you, you go to your doctor wouldn't you? [yeah] And he'd say
488 probably - probably say you're suffering from gout. [right] And you've never heard of
489 gout. [okay] I don't know. It's difficult.

490 PC: So you've not had erm sort of information about other conditions may come associated
491 with it or...?

492 F: No.

493 M: No, no.

494 PC: No one gave you information on that. Okay. Okay. Right.

495 M: Do you put your gout into a form of arthritis though or...?

496 PC: It is a form of arthritis, yeah. [yeah] Yeah, it's an inflammatory.

497 M: And you know so from that if you put it down to bone pain, do you put it all down to
498 gout or can you say there's an arthritic sort of component of the bone pain?

499 PC: So gout can co-exist with other arthritis, and particularly osteoarthritis or wear and tear
500 arthritis, so actually you know a lot of the times it maybe gout but it may equally be your

501 osteoarthritis which is causing the pain. And it's often thought to be a sort of vicious
502 circle where one sort of exacerbates the other. So...

503 M: Yeah, but if you've crystals deposit then you're going to get rubbing around aren't you?
504 [yeah] Well one would think you would. That's what I'm saying, if you've got high uric
505 acid, are you right knocking that down really, [yeah] so it stands less chance of getting
506 more precipitation in the joints.

507 PC: Yeah, no, that's true. Which is why we often wonder why people don't take long term
508 treatment because the whole aim is to get rid of the crystals. And things like ibuprofen,
509 although they calm down the erm swelling and the pain, [yeah] they don't get rid of the
510 crystals.

511 M: Mmm, no. I mean I do agree with that, but erm I mean obviously if you drink more, and I
512 think you do sometimes [29:11] a bit, do people get gout in the desert, I don't know.
513 Erm but you know...are other races more prone to it? I don't know. Is there a racial
514 element to it?

515 PC: Erm I don't think there is any particular sort of, you know, there are risk factors like you
516 said for alcohol intake and red meat and so on, and I don't think it matters whichever
517 race if you do that, then you're more predisposed to gout really. So...

518 M: [29:38] disease is racially prejudiced isn't it?

519 PC: Yeah.

520 M: So it's a form of erm...

521 PC: I guess you could say in that way, diabetes is more prevalent in Asians and [29:48].

522 M: Yeah, type 2, yeah.

523 PC: Yeah, yeah. Yeah. So yeah there are...

524 F: I've got diabetes.

525 PC: Have you?

526 F: Yeah, but only slight. [right] Because all my life, when I was younger, I used to have piles
527 of sugar, [right] three teaspoonful in a cup of tea, and my mother said you'll suffer for
528 this lady. You know. But I'm only tablets a day.

529 PC: Yeah that's erm - thank you for bringing that up, Margaret, that's interesting. Has any -
530 like do you have family members who have gout actually?

531 F: I don't...

532 M: No, I'm the only one.

533 F: What did you say?

534 PC: Did you have family members who suffer from gout?

535 F: Only my brother. [your brother?] He's in agony, our Robert is.

536 PC: You said, yeah. Right. [yeah] Okay, okay.

537 F: It can go months and not bother you. And then it flares up.

538 PC: Yeah, yeah. Is that - and that's - I suppose that's in a way a problem with this condition
539 isn't it, that you don't know when it's going to affect you really. Unless you figure out a
540 pattern that you do this and then it comes on. So...

541 F: You don't know do you?

542 PC: Yeah, okay. Anything else that you want to add about the treatment aspect?

543 F: [31:08 - off topic] No, I don't think so.

544 M: I don't really know.

545 F: No, I don't think so, just keep taking the tablets. [laughs]

546 M: Or not in my...

547 PC: Or not.

548 F: Or not in your case.

549 PC: Yeah. What - so if you had to go on - on a long term treatment for it, John, how would
550 you feel?

551 M: I don't think I'd be terribly bothered really. I'm not sort of erm...but I enjoy taking as
552 little as possible [sure] [oh yeah] and chemicals really, as I think everybody does, I mean
553 nobody really wants to be erm you know erm on things, [no, no, no] yeah, and I think -
554 erm I feel very content at the moment with everything really, I feel pretty fit, I wander
555 around, [okay] I see a lot of people a lot worse, whereas I'm contented really, and I think
556 that's the thing.

557 F: Oh yeah, a lot of people a lot worse than us. [yeah] Aren't there?

558 PC: Yeah.

559 M: I mean had I been 20 I might have sort of thought about doing it, but I'm not.

560 PC: Okay. So age is sort of an influence?

561 M: Well I think it is, I think you know if you're as fit as the rest of the people around you,
562 yeah, okay, or fitter than some of them I think.

563 PC: [laughs] Okay. Okay. Erm okay, well thank you for your thoughts on all of that, erm...and
564 anything before we finish off, Margaret, any thoughts?

565 F: No, no. no, not really. I just - you know, I thought there'd have been more people here.

566 PC: Yeah well unfortunately...

567 F: But like you said, because I'm sure there's people who have got gout.

568 PC: Yeah, yeah. [you know] Yeah.

569 M: Some people are afraid [32:45].

570 F: They won't come will they?

571 M: They shy away from it.

572 F: They won't come.

573 M: Instead of...

574 PC: Because of the gout do you mean or...?

575 M: Yeah, well with anything really, they think oh, instead of getting involved, [yeah] and...

576 F: You don't know what you're coming in to when we come here. [right]

577 M: ...they'd rather sit back and suffer in a way.

578 PC: Yeah, okay. Well no, thank you for - for your time and it's been really useful, so I'll just
579 turn these off and then we can [right] have a chat. [right]

1 **Focus group transcript 3**

2

3 PC: = MODERATOR

4 M: = MALE PARTICIPANT

5 F: = FEMALE PARTICIPANT

6

7 PC: Right, okay, so erm really what we wanted to do today erm is get your views and ideas
8 about how gout, and particularly its treatment, affects you, and your quality of life
9 overall. So you know feel free to start, anyone can start, and we'll all join in. it's really
10 sort of having a chat between yourselves rather than me asking questions if that's okay,
11 and it would - I just want to get out of all of you what it means for you to really have
12 gout and particularly focusing on how the treatment of gout has affected you, or if it
13 has, or you know - so yeah...

14 M: Well it affects me all over my body. Erm most people get it I find just in their feet or
15 whatever, but mine lies all over my body, everywhere. From one to another. [right] All
16 down one side, well everywhere.

17 PC: Right.

18 M: Well I started with it in my heel, and I went to the doctors and my heel was all inflamed,
19 [right] and he said I don't know what it is, you'll have to go for an x-ray. [right] So I went
20 to Allonton Cottage and had an x-ray, and it turned out it be gout. But they couldn't find
21 nothing on the x-ray at all. And then I got it in my fingers, one - and then I've just started
22 to get it in a toe.

23 M: I seem to have got off lightly, just one big toe. [right] I've had it for about 20 years, erm
24 and erm...when I found out it was gout I changed my lifestyle and stopped drinking the
25 things that I was supposed to like no red wine, not so much beer, red - eat more white
26 meat than red meat, did all the nonsense, and it seems over the years to have got a little
27 better. Erm I find it quite manageable with erm anti-inflammatory tablets I take for it,
28 [okay] along with the gastric tablet for the tummy, yeah.

29 PC: Yeah, to protect it, yeah.

30 M: Erm and I went to the doctors and asked if I could go on the one a day tablet for the rest
31 of my life job, [yeah] and she said the count wasn't high enough and I didn't have
32 enough reoccurrences of it in a year. [right] I usually get on average two a year, one bad
33 one that lasts for probably two weeks, and then one small one that lasts for two days at
34 the top whack. [right]

35 M: I think the main one I get, it's mainly more taxing than anything is erm - is erm in my left
36 toe, you know, the knuckle of the toe. [yeah] I think I had that - I think the first time I
37 was about - it came when I was about 28, 29 when I first had an attack, and first of all to
38 be quite honest with you I got up in the morning I thought I'd kicked the bed, I didn't
39 even know what it was, and I thought I'd sort of kicked the bottom of the bed or
40 something like that, you know, the foot of the bed, it was that painful like, I went to the

41 doctors and she said well it could be gout, so I had that. And then I didn't have anything
42 for about three or four years, anything at all like that. [right] Just went. And then I had
43 an attack and I thought [3:20] this is, and then as I've got older it's - it's been more
44 frequent in that toe. I have had a touch of it in the right one, but I've never had it since.
45 But there's - it's just things that you try to I'd- I mean I've tried to identify what triggers it
46 off really, and I think it's if I have a lot of something, too much of the one thing, it
47 doesn't have to be beer or alcohol, it can be one particular thing, that...

48 PC: You mean anything, food or...?

49 M: Could be food, could be food, anything, you know, and erm if I get - if I get I get times of
50 things when sort of I enjoy eating that, so I'll have a lot of it like, you know I'll have that
51 again and again and again. And that'll - when I should you know - and that will trigger it
52 off. I mean as I was saying earlier, the one summer I was working in a massive garden
53 and did all the lawns and everything, a red hot summer, so I had a glass of orange juice,
54 and enjoyed that, so I had the whole carton of orange juice, [right] the next day I
55 couldn't walk. [Really?] Mmm. It was...

56 M: I'm inclined to agree with you. [yeah]

57 M: Yeah I know I kind of guess when I might be getting one, [yeah] by the fact that I've over
58 indulged somewhere.

59 M: Yeah, the same thing all the time.

60 M: But - yeah, by well yeah, sort of you know maybe I've been out for two or three nights
61 and [yeah] - I don't say to the pub, I don't go to the pub that often, but if I've been
62 drinking two or three nights, [yeah] a bottle of red wine each night, maybe the next
63 week something will happen. It doesn't always, but [yeah] I feel susceptible to it.

64 M: I'm not - I mean I don't drink, I don't - I'm not a big drinker, I'm not a drinker at all really,
65 I do have a drink, but I don't class myself as a drinker like my friends are drinkers, do you
66 know what I mean? [right] So...

67 M: And they don't have gout?

68 M: Some - there's one now that does, but I know one who's a big drinker, Neil, he's a big
69 drinker, and he never has a thing of it. You know, so I've dispersed this thing about
70 alcohol, I just [5:01].

71 M: Well I get it in my ear.

72 PC: Yeah.

73 M: The ear?

74 PC: Yeah, that's also known to have the [5:08].

75 M: Is it? [yeah] I didn't realise. [yeah]

76 M: But I had bypasses oh 15, 18 years ago. And where they took my vein out of my leg,
77 [yeah] I used to have erm what do you call it, they said it was nerve endings...

78 F: Like an eruption it was.

79 M: And it would never heal, never, I used to put cream on it, every day I had to. [yeah] But
80 if that comes now, the gout goes.

81 PC: Right, okay, okay. So how did the whole sort of process of, you know, getting diagnosed
82 with gout make you feel in the first place? Was it something that shocked you like that?
83 How did you feel? How did it...was it a long drawn process or unexpected or...?

84 M: It was a shock.

85 M: When I first got it, like I said, I felt like I'd sort of got up in the morning and I'd banged
86 my foot, I thought I'd done, you know, kicked the floor, the bed, the leg of the bed or
87 the cabinet, and it feels like that. And I thought I don't remember doing that. So I went
88 and - you know, [6:07] then I went to the doctors, and the doctor he looked at it like and
89 you know yes, I think you've got gout, because it sort of glows and it's hot and it sort of
90 shines and all that, and everybody says you've got gout. Then it went away, because I'm
91 quite active and sporting like yourself, then and I still am, and I was then, and erm - and
92 it went away and I forgot all about it and then after about as I say four or five years,
93 maybe longer, it just came on and the attacks have been more of erm...you know, more
94 regular then, but it's - I think with me I think what annoys - it's in your feet, like you're
95 standing on your feet all the while, [yeah] and just to get a shoe on, [yeah] you know
96 you feel like you've got the wrong - I mean whatever foot, it's like mine's in my left foot,
97 I felt I've got the wrong size shoe on, you know, I mean I thought, you know...

98 M: Well I couldn't get my shoe on, last - a week ago since my last one. [right] I couldn't get
99 my shoe on for three days.

100 PC: Okay, I see. That's like you as well?

101 M: But the shock was saying I've got gout and straightaway it's with the well off people and
102 [that's right, yeah] and the rich food and...

103 M: That's right.

104 M: I don't have that food.

105 M: Port and pheasant they say don't they?

106 M: Yeah, yeah.

107 M: Probably drink too much port and I don't drink. [laughs] I don't drink. [yeah]

108 PC: Right, yeah, so it's interesting how other people [that's right] perceive it as well.

109 M: That's how it's perceived as gout, you're rich [yeah], you're a rich or wealthy person. And
110 you know, but it's not at all, I mean I've...

111 PC: And who's that from then? Is that your family or friends or...?

112 M: Everybody.

113 PC: Everyone, right.

114 M: Everybody. Everybody, I mean I eat - I'm not - I've never been a flash, because as I say
115 I've always lived like - I've done athletics all my life, and I've never - I've never been sort
116 of - I wouldn't spend money on expensive food and rich foods anyway, I've never done
117 it. It's the way I've been brought up and I've never spent money on drinking, I mean if I
118 have a drink it's only beer, so I don't drink port or wine or brandy or whisky or anything
119 like that, it's just beer. [yeah] But the one time I had it, luckily it's only the once, it was - I
120 had a pint of cider, and that's - that triggered it off. I'm sure it did. I went on the
121 Saturday, had a pint of cider, I had one pint of cider Saturday because I had to be up
122 early on the Sunday, and I had one pint of cider, and I got up on the Sunday and it
123 was...things [8:28].

124 PC: Right, so - so coming back to the treatment aspect then, obviously when you did get
125 diagnosed with gout, how quickly did the treatment happen? So what were your
126 experiences of gout treatment? Let's talk about that.

127 M: Erm I...

128 M: With me it's about three or four days when it - with the tablets.

129 PC: So what, what do you mean, Ray, three or four days, to clear it or...

130 M: To clear it, clear [8:55] you know it's start clearing and [okay] and then perhaps four or
131 five days it - I'll be able to get a shoe on.

132 PC: Okay, and what tablet do you take for that then, like initially?

133 M: Oh I don't know what they are.

134 PC: You get it off your doctors do you?

135 M: No, I have [9:09].

136 M: I know I have [9:10].

137 PC: It's a painkiller is it?

138 M: It's erm...[9:16] yellow.

139 PC: Right and every time you get an attack, do you go to your doctors or do you just...?

140 M: No I just treat myself now.

141 PC: Right, and where do you get those tablets from, you just have them in stock do you?

142 M: Yes, from the whatsit, the chemist.

143 PC: Oh the chemist.

144 M: I go for my prescription off the doctor, [yeah] and I - I go to the chemist and get them.

145 PC: Right, so your doctor puts it on your prescription?

146 M: Oh yeah, yeah.

147 PC: Right, okay.

148 M: Well I started off with Diclofenac. [right] For a good long - for a good many years.

149 PC: Okay, and how was that for you? Were - were you satisfied with that or...?

150 M: No, no good, did nothing for me.

151 PC: Didn't do anything?

152 M: No, no, so then I went onto - what was it?

153 F: Allopurinol.

154 M: Allopurinol.

155 F: Allopurinol was - because they are a management thing, tablet, more so than like erm a
156 painkiller aren't they? [yeah] But then you had side effects with Allopurinol, [oh aye]
157 erm he took one every day didn't you, of that? [yeah] And then his head was bursting
158 and oh it was awful. So...

159 M: Cocodomol now, I take cocodomol.

160 PC: So cocodomol helped?

161 M: It helped, yeah. Yeah.

162 M: They offered me one you can take - you can either - he could prescribe one to have one
163 every day like for the rest of my life, he says but [yeah] and he says I wouldn't really
164 recommend it if you can get away with it, I wouldn't recommend it and just come in if
165 you start getting an attack like, you know, sort of...

166 PC: That's interesting, and so who told you that then?

167 M: Well my doctor, my doctor.

168 PC: So they said that you don't need to go on it?

169 M: He said I wouldn't recommend it, you know, he said I'd rather - and he asked me would
170 you like to take a tablet every day of your life and I says not really, no, like you know I
171 really wouldn't want to be on that sort of thing, I said I'd rather stick to it where I can
172 have a tablet and get it, you know, and have a supply if I can feel it coming on, because
173 I've got a spare box at home like, you know what I mean, that [11:03], so when I feel this
174 thing I feel I can get them and try and beat it.

175 PC: And why is that, why are you not keen on going on a tablet every day?

176 M: I don't know, I just got that thing about it, I think it's just a...

177 M: He's sick of tablets like me.

178 F: [11:20]

179 M: Yeah, it's [11:23] I've got that impression I just don't want to - if I had to I would like, you
 180 know, but at the moment I think I'd rather be able to manage it the way I'm doing now,
 181 you know. It's...

182 M: I think where you start with doctors or hospitals, you're never away. I'm never away
 183 from the hospital or doctors. [no] [no]

184 F: But that's just your experience ain't it, because he's had a lot of things. [yeah]

185 PC: What about you, Ron?

186 M: I erm...I found I can manage it, erm the only problem in my head is if I was going on
 187 holiday the next day, it would be a bit of a struggle but I'd get there somehow. Erm but
 188 how I manage it, I mean it always comes on in the middle of the night, and wakes me up.
 189 And I know what it is straightaway, because the covers make your feet hurt, and it
 190 pulses and things are going all funny. And erm I just get up and get a duvet and go and
 191 sit downstairs, take the tablets, I take erm - I think it's the same one you said, erm...but
 192 it's an anti-inflammatory tablet basically, [right] erm with a digestive cover for it, [yeah]
 193 erm and I get an icepack, bung it on my feet and I just sit there for about four or five
 194 hours, and it then becomes tolerable. Erm depending whether it's a bad attack or a mild
 195 attack, erm the next day I keep my leg up and that on, and fort because I've finished
 196 work only I can do that, it's not a problem really, erm...after - the milder attack, after the
 197 end of that day I can probably get back to walking around fairly well and a day later it's
 198 pretty much gone. Erm but the bad attack will last maybe two or three weeks
 199 afterwards, erm the swelling stays there, erm right into the second week, erm and I
 200 can't get a shoe on. Erm...so I can't really go anywhere or do anything in that sense.
 201 Erm...and I keep the tablets up a length of time, and I do keep a stock of tablets at home
 202 [right] ever ready just in case, and I take them with me when I go on holiday and stuff
 203 like that.

204 M: That's what I do, sort of stock up on them just you know, just sort of...

205 M: Yeah, I try and...

206 M: Just in case.

207 M: ...in case you're going away.

208 M: Well I do feel now I can manage it in that fashion, erm I did ask about erm taking the
 209 one tablet, but the count wasn't high enough and I didn't get it often enough the doctor
 210 said, but I had a feeling what you said, that erm maybe she didn't really want me to take
 211 it for some reason. Erm...

212 F: Was your doctor reluctant to send you to erm a gout specialist shall we say? Has the
 213 doctor always managed it?

214 M: I've never got anywhere near that. Erm...[oh] my - I moved here six years ago, so my first
 215 gout was elsewhere, erm and basically the doctor just said well we'd better find out if
 216 it's gout or not, blood test said it is gout. Fair dos, no problem, I looked it up on the
 217 internet and had a good sort of investigation myself into it. Erm...and erm the only
 218 reason that erm I went back this time to - to see about it was the fact that I was a little
 219 bit frightened if I was going to go on holiday the next day it was going to clobber me that

220 day, you know. [yeah] So I thought - and I'm old enough now that another tablet for the
221 rest of my life doesn't make a lot of difference, so you know...

222 PC: So you're not sort of adverse to the idea of taking something everyday?

223 M: No, no, no. not at all.

224 PC: Right, okay. Yeah.

225 M: I'd like to know the side effects though, properly [yeah] from a doctor, and not from the
226 internet.

227 PC: Yeah so that's interesting that you said you went on the internet to investigate for
228 yourself.

229 M: Yeah well I - I was looking to see how I should change my lifestyle because I think I said
230 to you I changed my lifestyle when it happened, because it was so painful basically,
231 [yeah] I didn't want that any more, erm and you know I found out that beer's got the
232 chemical in, the acid in, so has red wine, erm what else was it? Smokey, erm oily fish has
233 got the chemical in as well. [yeah] And they're all things that, you know, you can do
234 without. A good cooked breakfast two or three times a week doesn't do you any good
235 does it? You know, so things like that. [laughs] Yeah.

236 PC: Okay.

237 M: [15:18] I had a list off my doctor and he - some of the things that were on there, you
238 thought...

239 M: Oh they put everything on there.

240 M: ...what am I going to eat? [laughs] What am I going to eat? [yeah]

241 M: You have to take it with a pinch of salt.

242 M: Even nuts they reckon, it was saying reading somewhere even sort of peanuts can bring
243 an attack, bring it on. [right] You know...

244 F: So - so you never had to have steroids or any fluids removed or any injections?

245 M: No, no, no.

246 M: No, no.

247 M: I have to.

248 F: See John's...in July it was a really bad month, he had it in his shoulder, his elbow, his
249 wrist, all the left side, his knee, and had to go to the Haywood and have fluid drawn off.

250 M: I can't get into bed, I can't move. I have to have a cage over my [15:55].

251 M: Oh I don't get anything like that.

252 F: But he's had a big operation, the aneurism - he had an erm aortic aneurism, and after
253 that he seemed to have gout every month, whether it's got anything to do with that, I
254 don't know. But he was really...

255 M: I think it had, [16:12].

256 M: But then again...

257 PC: You think it has? [mmm]

258 M: ...if and when I go holiday to a warm country, either India or to erm Egypt, [right] I don't
259 have any trouble.

260 PC: No?

261 M: No.

262 M: No. no, so I don't know whether it's...

263 M: I think it's the dampness. I - I...

264 M: I don't know what it is.

265 M: I watched a programme once and there was this - there's this - it was gout, but he
266 suffered with kind of arthritis, and he lived in this country and he was 16 or 17 and he
267 was dying with this arthritis. Remember that, it was years ago. And I was watching it and
268 the doctor turned and he said to the family if you want - if you want him to erm - your
269 son to live as long as possible, get him out of this country. [right] Because the damp
270 weather [yeah], the cold and damp weather, is just not helping him at all. [right] And
271 they moved, they sold up and they moved to warmer climates, like Spain. [17:04] And
272 his life continued.

273 M: [17:05]

274 PC: Sorry, Ray, say that again.

275 M: I don't think there's many [yeah] what haven't got arthritis in this country, [really?] with
276 the weather we have. [yeah]

277 PC: Mmm, so you think it's quite a common...?

278 M: I think it is, I mean it's...

279 M: Everybody has got it. [yeah] I don't know who hasn't got it.

280 M: I was going to say...yeah.

281 PC: You mean gout or arthritis?

282 F: Not gout.

283 PC: Oh just arthritis, okay. So...

284 M: Well gouts a form of arthritis.

285 M: It's borderline.

286 PC: Well yes, I was going to - that was my next question, so how do you differentiate it.
 287 Okay, right erm and before you all sort of had gout diagnosed yourselves, were you
 288 aware of much about it, so what it is or how you treat or had you come across it?

289 M: No I've never heard nothing.

290 PC: Never heard of it?

291 M: No, I haven't [no] any road.

292 M: I had a - I had a colleague at work who had gout, but he was 65, just about to retire, and
 293 he was rather portly and he drank a lot, he liked to drink a lot of wine, all the things you
 294 were saying, he did and so you know that was how he got it, you know, that's why
 295 you've got it.

296 M: I don't know whether it's hereditary or not but my - my [18:11] but my granddad used to
 297 have it you see, apparently. [okay] So I don't know if it's hereditary you see, whether
 298 it's...it's...

299 M: My family were all arthritis. And none of them have had gout, but they've had arthritis
 300 badly. [yeah] My father and everybody. [right]

301 M: But you go on, I also read if you go on, that was about what can also contribute to it's -
 302 see it's what you read, [18:35] fascinated really when you've got something that annoys
 303 you, it affects your lifestyle, you know, it really does, [it does] because when you can't
 304 walk, I'm a long distance runner, so when I can't run like I hate it. Really you know
 305 messes me up really. Because it always comes when I've got a big race, but anyway so...I
 306 read - and they reckon your kidneys as well, because your kidneys break your food down
 307 and this is why [19:00] if I enjoy I'll have that, I'll have that, and I'll eat a lot of it because
 308 I enjoyed eating it, and your kidneys can't handle breaking that food down quickly
 309 enough. [right] Which could bring it on as well. I don't know, it's only what you read isn't
 310 it, you try and find out to try and cure it yourself.

311 PC: And do you find these sort of things out from mainly other people, internet etc., or do
 312 you...?

313 M: I go on the internet, have a look on the internet now like.

314 PC: Internet. You don't talk to your doctor about it?

315 M: Well we have a chat with him like you know when I erm - [yeah] and he just gives you -
 316 you know, he says well try and just change your life and your food, [okay] but it's very - I
 317 mean with my job like with working away it's very difficult to manage your - you know,
 318 [19:36] [yeah] so I you know - it really - you're working until 5 or 6 o'clock, and then you
 319 go and grab something to eat, and then back to the hotel, and you're - it's just so
 320 difficult, it is.

321 M: But you couldn't talk to my doctor about it, he wasn't interested. He would never have
 322 let me go to erm...

323 F: The gout clinic.

324 M: The gout clinic. No. until I went for this aneurism, and I asked the doctors in the hospital
325 and they referred me to erm - and that's how I got to go there.

326 PC: Right, and why is that then, John? Why were you - why do you think people are
327 reluctant to send patients...?

328 M: Because he said I'm managing this, you're all right, don't worry.

329 PC: Right, okay.

330 M: But I was never rid of it, I was down all the time, and...but he'd never send me up there.
331 [right] So I could see erm the specialist.

332 PC: So would you say overall you're happy with the treatments you're on for it? Or if not,
333 then what else do you want it to do for you?

334 M: I'm happy that I can manage it, but I'd love to find something that makes it go away.

335 PC: Completely you mean? And never comes back?

336 M: Yeah, yeah. Yeah.

337 M: I would like something to manage it. [yeah] [right] I've got no tablets at the moment,
338 nothing.

339 PC: You've got no tablets at the moment?

340 M: Nothing, no.

341 F: He's had to come off them mind you because [oh right] the tablets that he does take,
342 because he's had these different problems, they conflict with some of the erm
343 management type tablets erm that he had, but erm...

344 M: So I'm waiting to see Dr. Roddy now, and he's going to change my tablets.

345 F: But he's tried the Allopurinol, he's had erm febustat, he's had erm steroids, and colchine
346 is a tablet that erm he takes now don't you?

347 M: Yes, and...

348 F: If it's coming on...

349 PC: Oh right, so that's your...

350 M: For a short period. [yeah] A very, very short period.

351 F: Yes, but it isn't a management thing, not the one a day, that's just like the...a little white
352 tablet that is.

353 PC: Yeah, yeah. So erm apart from getting rid of the pain or you know the swelling, you want
354 to clear it completely, you want the treatment to [please] [oh yeah, I do] take it away
355 completely.

356 M: It's the unpredictability of it, you know, [yeah] [right] you make a plan to, I don't know,
357 maybe go to theatre in five weeks time [yeah] and when it gets closer you think god, I
358 hope I don't get gout just the night before I go.

359 M: I'm like that.

360 M: You know and whatever you're doing, you know, except for everyday things that can be
361 put aside, erm when you make a commitment, you feel nervous that you're going to
362 have an attack.

363 PC: Right, okay.

364 F: There isn't erm...what can you say, an emergency thing that you can take, like you feel
365 oh, it's going to come on, erm and then it comes on. And it's that [22:24] that you really
366 bang your head against the wall and you - there isn't anything that'll take that off for a
367 day perhaps, when it sort of goes a little bit better. I mean yours is for a week.

368 M: I mean the...

369 M: The tablets that he's given me I take them every day.

370 F: Yes.

371 M: So you know I still get it.

372 M: I think it's still looked at as what I said earlier, the old wives tale, the port and pheasant
373 and I don't [yeah] think there's not enough people coming - there's more people than
374 what we think who get it a bit, [22:52] not coming forward and saying this is a bigger
375 serious problem than erm [you think] than what you think, you know, you talk to people
376 and say oh I get that, what do you do about? Well nothing. Well if you're doing nothing
377 nothing will ever happen about anything will it?

378 PC: No. so why's that, why don't people come forward?

379 M: I think just - well it's the old wives tale thing like they say, they just think it's port, they
380 think oh, it's rich living, that's all it is, and it isn't, it isn't rich living.

381 M: Well my neighbours still think that.

382 M: Yeah, people do. And they really do and they think oh it's drinking beer, stop drinking
383 beer and it'll go away and it's not that.

384 F: Yeah, no, you don't drink.

385 M: I don't drink.

386 M: It's not - I don't drink, but I drink once a week, you know, and that's it.

387 F: He [23:26].

388 M: I have a sherry. I go to the gym when I can.

389 M: Same as Charlie earlier on, my doctor didn't know what it was [yeah] when I got it in my
390 [23:33], [yeah] he sent me for x-ray. [right] And of course that was blank, [yeah] and
391 then he decided it was gout.

392 PC: Right, so was there much of a delay in you getting...

393 M: Well there was a delay, knowing what it was [yeah] from the x-ray, you know.

394 PC: Yeah and how did that make you feel? How did that make you feel?

395 M: Oh I just told him off. [laughs] [right]

396 F: Frustrated as well.

397 M: Simple as that.

398 PC: Frustrated, yeah, yeah.

399 M: He just laughs it off he do.

400 PC: Yeah okay. And has treatment had any great impact on the way your life has become
401 now, like are there things you can do or can't do or how does it affect your lifestyle in
402 general or quality of life?

403 M: I think it...

404 M: When you've got it, it does doesn't it?

405 M: Yeah I mean what it is it's the unexpectability of whether it's going to come on or not.
406 You know, there'd be nothing worse than being on holiday somewhere over in the other
407 side of the world and it comes on, you know, and that's - you're thinking oh my god, it's
408 coming on again. You know, [24:35] basically, especially if it's in your feet and you can't
409 even get about anywhere, it's that unpredictability of whether it's going to kick in or not,
410 but like you say you're in the warmer climates you're okay.

411 M: You haven't got no quality of life though have you?

412 M: No.

413 PC: You haven't got a quality of life?

414 M: I can't do nothing, I can't go anywhere.

415 F: When you've got it, no.

416 M: I can't go.

417 PC: And how does it affect your sort of interaction with others or work or you know things
418 like that?

419 M: Well I don't work. [okay]

420 F: He's retired, he's 74. [right]

421 M: At work like if I'm walking round [25:09] and I've got it like it's a bit awkward, you know.
422 But I can manage to still do my job, you know. Like it's office work now, like you know a
423 desk job now, but if you're on site you have to walk and I've got it, but it's only
424 happened ever once, you know. So I had to struggle with it, you know, then I just tell
425 them, I'll say my foots hurting, I ain't going to walk around now like, you know, I can't
426 put it on. Because if you've got to put your boots on or something like that, you go...it's
427 sort of...so you...it's just - it does, as you say if you knew it was going to do something
428 straightaway, but you can't, it's like I'd go to the doctors, I'm in the doctor on Tuesday
429 because I've got an attack now, but I've already got a load of tablets which I'm taking
430 them, so I've got to go in Tuesday, because you have to book an appointment these days
431 don't you, you know what I mean? [yeah] You know, so it takes three, like it can take
432 five days to see my doctor. You know, so by the time I get in there it'll probably have
433 eased down a lot then and I'll say well I did have it, [yeah] so I will still go in there and
434 get a prescription of tablets.

435 M: We could do with a point that we could phone and say, you know, I've got it [yeah] can I
436 come and get treatment.

437 PC: Right, so something a bit quicker, like [oh yeah] an instant sort of...

438 M: Yeah, aye, got to wait to see your doctor or whatever. [right]

439 M: Yeah, see it's five days like, you know, to see my doctor.

440 M: My doctor, Dr. Rodd, he's very, very good, he'll say come up.

441 F: That's at the clinic. [yeah] That's going to the, you know, the gout clinic. [oh] [yeah] And
442 that's a job to get there, with most GPs.

443 M: It is.

444 PC: Right, okay.

445 M: Yeah, although [26:31] everywhere aren't they? [right] Yeah.

446 PC: So you've all talked about how gout has affected your quality of life, what about the
447 treatment, has that had any impact on your quality of life?

448 M: The only - I mean the only thing I find is erm I feel a bit offside when I'm taking the
449 tablets. And there's a temptation to stop too early, taking them. You know once it sort
450 of dies down, you're supposed to take them for another two or three days after, and
451 there's a temptation not to take those few you know.

452 M: [27:00]

453 M: Well it doesn't matter about the [27:00], it's just the fact that you feel so offside that
454 you [right] you know, you just want to get rid of that sort of sick feeling, [yeah].

455 PC: Right, what about you Ray and John?

456 M: Pardon?

457 PC: How - what - how do you feel about the treatment, does that cause much of an impact
458 on your life or...?

459 M: Not - I don't have any treatment really as such.

460 F: No, but over the time.

461 PC: Or when you used to. [pardon?]

462 F: Over the years you've had different tablets and they've made you poorly.

463 M: I've never had anything that will shift it within two or three days, never.

464 F: But how has the tablet reacted against you, that's what the doctor's saying.

465 M: I get a lot of headaches, really.

466 PC: Right, so you get problems with them.

467 M: I can't sleep. I'm up day and night and I can't sleep at all.

468 PC: Mmm, what about you Ray?

469 M: I'm all right, I am, with the tablets.

470 PC: Yeah, okay, okay.

471 M: Is there different types of this gout?

472 PC: Sorry, say it again.

473 M: Is there different types, everyone's on different tablets, so is there different types?

474 PC: It's - there are lots of treatments for it and erm you know it depends on what suits one
475 person, it may not suit another person. So that's why people are under different
476 treatments. And then obviously as you've all pointed out, there's the sort of the
477 management in the really acute...

478 M: So why over the years haven't I had these treatments?

479 PC: Well you've had different treatments.

480 M: What have I had? Aspirin?

481 F: No, you've had erm Allopurinol, then you had...

482 M: [28:22]

483 F: Then you had [28:22] - then he's had Allopurinol [yeah] again, then you've had steroids,
484 then you've had colchine, but because of the other medication that he takes, the gout
485 tablets don't sit well.

486 M: Within days I get a headache, I can't see. So...

487 PC: And have you all found that to be true, like does - do your gout tablets cause a problem
488 with your other tablets if you're on anything else?

489 M: No, I sort of just take them I do, I sort of just carry on as normal really. You know, apart
490 from the pain in the foot. [yeah]

491 M: Yeah, I've had no problems, I mean I take erm - erm... [28:58] for high blood pressure,
492 [okay] which isn't high any more but I still take it. And erm - oh dear, I've forgotten the
493 name for this thing now, the thing that blocks up your veins...

494 PC: Cholesterol tablets.

495 M: Cholesterol, I take a cholesterol tablet as well. [yeah] And have no problems at all with
496 those when I'm taking the gout one.

497 M: I haven't got no problems with mine.

498 PC: Right. And do you know much about sort of how gout is related to other medical
499 conditions or has anyone explained how it maybe related to anything else?

500 M: No.

501 PC: John, probably.

502 M: Just my tablets, that's what they put it down to.

503 PC: You put it down to the tablets? [yeah] Right. Okay.

504 M: I mean I've been to two different doctors, one where I used to live in Lowestoft and one
505 in erm Woolstanton now, and erm neither doctor has really done any explaining or
506 anything else, they're just sort of take the tablets when it comes on, erm and I've just
507 really dug things out myself, what it's about and why.

508 M: That's all right if you [30:05].

509 M: I'm not - that I wanted them to tell me particularly, but you know...

510 PC: Why not? Why did you...?

511 M: Erm because I can find out myself.

512 PC: Right.

513 M: Just, you know, talking to other people and the internet etc.

514 PC: Is that something you prefer over getting...?

515 M: No I don't prefer it but I think it's better with gout because no one seems to know why it
516 starts, who it starts with, there's about ten different probabilities, you can have it once
517 and never get it again. [yeah] And you can have it when you're 20, or you can have it
518 when you're 70 odd, erm it can start then I mean. And you can have two or three attacks
519 and it goes away. Erm or you can have an attack every five years. You know, it's - no one
520 really seems to know. And you ask what - you know, or you try and find out what causes

521 it, erm and you get a list as long as your arm, you know, you'd never eat again if you
522 weren't careful. [no] [right] You have to use a bit of common sense.

523 PC: Right, yeah. And what do you to, all of you, do to prevent it coming on, is there a
524 particular regime or things that you, you know, you do?

525 M: I think it's just [31:09].

526 F: It's just food isn't it really?

527 M: Yeah just keep off the wines and beers and stuff like that.

528 F: But you've never drunk.

529 M: No, no.

530 M: I enjoy drinking orange juice, but [31:16] that. [yeah] I just keep off it. You know, orange
531 juice.

532 M: I can drink a spirit and I - I can drink whisky, I love whisky and I drink whisky and it
533 doesn't bother me.

534 M: Yeah, I'll have a sip, a little small glass of orange juice, but I won't sort of a large-ish,
535 whatever, it's - to me it just seems if I have a lot of one thing whatever it is, it'll bring it
536 on.

537 F: But you do everything, like John has erm cherries every morning [yeah] with his
538 porridge.

539 M: I have cherries. And I have seeds sometimes, celery seeds.

540 F: He has erm celery capsules, people say that...

541 M: And I think that helps, it does.

542 M: Cherries do, I've heard this guy, this architect, he said cherries like, you know, he
543 recommended cherries.

544 M: But [31:55] to learn, nobody else tells you anything what to eat and what will help. [no]
545 You don't get that.

546 PC: No, how do you think that...

547 M: I was talking to a doctor...

548 F: Yes, well [32:06].

549 PC: Yeah, I was going to ask you actually. How do you think that we can improve the
550 management of gout then? Because it doesn't seem like you know you've...

551 M: I don't know whether you can manage it. [laughs]

552 PC: Say it again Ray, you don't think...

553 M: I don't think you can manage it.

554 PC: Why do you say that?

555 M: Well same as I say, I went to my doctor, he didn't know what it was.

556 PC: Yeah but erm so how can we improve on that?

557 M: Well I don't know. I'm not a doctor. [laughs]

558 PC: Okay.

559 F: Probably give you more information about the diet and...

560 M: What causes it anyway? Can you tell me that? [no]

561 PC: Yeah well I can tell you that but we'll talk about that later. I just want to find out your
562 views first.

563 M: I think mine is like it's just the same is managing what I eat, and watching what I eat and
564 [32:52], that's the only thing I can put it down to, what'll bring it on, is what I eat, and
565 too much of the same thing will bring it on.

566 M: Have you changed your diet though over the years?

567 M: Yeah I keep trying like, you know, but I mean you get so - I mean I'll be quite honest, it
568 gets so boring like. You know what I mean? [mmm]

569 F: He don't have steak, he don't have beef.

570 M: I try not to... [33:09]

571 M: I don't eat beef, I don't eat much red meat.

572 F: No, we don't.

573 M: I don't eat much red meat, I just have a little bit and sometimes I go out and my mates
574 will have this and I'm thinking shall I have it or shan't I have it like? You know, and this -
575 and it's like - and you're sitting there and thinking I'd love to, but I daren't eat too much
576 just in case, you know. And I just try to - it's the quantity of the - I think, it's only my - too
577 much of the same thing, too much of the same thing.

578 F: So variety is your...

579 M: A lot of variety. Small bits of variety, like a little bit of meat, and I think - that's my own
580 personal opinion, but I think - but I'm a sucker for well I enjoyed eating that, I'll have
581 that again and again and again. I'm a sucker for that. You know. So it's - I think it's the
582 food, it's what too much of the one thing and your kidneys go what's all this? They can't
583 handle all this, so that's what I think, but it's so difficult, you know.

584 F: So what you're saying what would help is if somebody could come up with we definitely
585 know that if you have steak once a week or twice a week or beef, it'll bring it on. Or if
586 you have prawns, you're all right. Is that what you feel?

587 M: That's what I think, you know, or not too much of it the same all the time, you know.

588 PC: But is that something that you think might happen in reality because obviously it's
589 different things for different people...

590 M: It's down to that...

591 PC: We would be - so are you saying perhaps that the doctors would have to then be very
592 individual sort of - for John, you can't eat this, for [yeah] Ron, you can't eat this?

593 F: Mmm, and I don't think you can. Can you?

594 PC: Right.

595 F: Because like I say, it's an individual thing. John [yeah] has what they call polyarticate,
596 which is in all joints, whereas Eddy only has it, and so does Ray, so you know Ron, erm
597 so it's very difficult isn't it, from the medical point of view to say you shouldn't have this,
598 but you can have this. [yeah]

599 M: Everybody is different aren't they in what we can eat and what we can manage. [yeah]
600 But I'm almost certain it's what we eat. You know, I'm...

601 PC: So is there - do you wish for example, Ray, you said your doctor didn't know what it was,
602 do you wish that, you know, what do you wish that they'd told you initially, or you know
603 given the information about or...is there something that you wished they'd done for you,
604 all of you really?

605 M: Food that erm...they feel...

606 F: Triggers it off.

607 M: ...could bring it on, i.e. with a high level of the erm acid in that food. A definitive list of
608 those things would be helpful.

609 PC: You wanted those? [yeah] Right, okay.

610 M: Yeah, I think. You know, you go on the web like and you get a list that long and you
611 compare it with the National Health Service list, and it's different.

612 F: Totally different.

613 M: You know and you think well I'm trying...

614 M: I think you'll find you try to eat your five a day until they say you can't can you? [yeah]

615 M: [35:57] all I've really done is my diet has become healthier and my lifestyle has become
616 healthier, [right] for various reasons, erm nothing to do with gout really, just for other
617 reasons I felt it was a better thing to do. [right] Erm and I eat things like I have a nice
618 steak maybe once a fortnight, rather than three times a week. [yeah] Erm I'll have a
619 glass of red wine, which I love, once every three months rather than a bottle a night, you
620 know. It's - it's - and I feel more comfortable with that.

621 M: And that's how [36:28].

622 M: I feel I'm doing something towards it.

623 M: And I go to the gym three times a week if and when I can.

624 PC: Would there be anything that made you sort of - apart from the side effects that you've
625 talked about John, is there anything that would make you stop treatment or start
626 treatment, any - any sort of particular features of gout?

627 M: I don't know, I think when you get it and you're in pain with it, you'll take anything.

628 M: You'd grasp at anything.

629 M: You'll take anything, you know what I mean, you'll take anything to get rid of it, you
630 know. It's - it's...

631 M: I mean the pain is...

632 M: I still think, you know, it's still - it ain't took seriously enough to be honest.

633 M: I'm taking my tablets everyday but it still comes back.

634 PC: Right, okay. Okay. And that - how sort of what do you feel about that then? Obviously
635 you're not...

636 M: I wish I could do without them really, [laughs].

637 PC: So would you consider stopping it if it's not working? Because from what you're saying
638 it's not working, is that right?

639 M: Well that's what I'm saying. It [yeah] comes back, [yeah] and yet I'm still taking the
640 tablets everyday.

641 PC: Why are you doing that? Have you considered just throwing them away because it's...

642 M: Well many a time, when I feel a bit low, you know, at times with it.

643 PC: You feel a bit...?

644 M: Low. [low] When you get it. [yeah] And you say well, I've taken my tablets and I'm still
645 getting it.

646 M: Do you think though if you threw your tablets away you'd get it more often?

647 M: Well...

648 F: He daren't.

649 M: Well what's it on, you're gambling aren't you? [yeah]

650 M: It gets me down.

651 M: Yeah, yeah. But someone should be able to tell you that if that's a fact or not a fact
652 before you make that decision. [yeah]

653 F: It gets John down, he gets really frustrated, [oh yeah] because he has it so many times.

654 M: Yeah I've tried...it gets that painful I'll cry. I can't get rid of it.

655 F: He's in the bath and his arms out and...

656 M: I'll get in - I'll get into freezing cold water and sit there. [yeah] I take that pain to take
657 that off, if that makes sense.

658 F: Then he has pads, he has heat pads.

659 M: Anything to just stop it.

660 M: I read somewhere and erm maybe I shouldn't say this, [no, no, no] [38:33] you are, they
661 reckon that the erm gout - someone reckons somewhere that gout is the second most
662 painful thing to erm childbirth. [yeah] [38:43]

663 PC: Yeah. That's erm...

664 M: And I actually believe that [right] from the pain that you get.

665 F: Only secondary from childbirth. [laughs] I assure you. Sorry.

666 M: I'm I've broke my foot in the past, I was a kid, and it was never as painful as gout, it
667 weren't as painful as...[really?]

668 F: No, I mean it is, I've seen John.

669 M: I broke my foot like two or three times, and it's sort of not as painful as that, you know.
670 If it breaks, [yeah] you go to the hospital, put it in plaster, and you're - a bit of a
671 throbbing and it's gone, but with gout it's bang, bang, bang for days and days.

672 F: You've got a very high erm threshold of pain haven't you really, because he's been in the
673 building industry a long time and he's, you know, really erm worked. But this...

674 M: Oh, it gets me down, in my wrist and I can't move, can't pick anything up.

675 M: When you get your gout do you - do you put erm - I've got a bag of peas specially made
676 [yeah] to go on my feet when it happens, do you do that sort of thing?

677 M: Mmm, I haven't no.

678 M: I find that really helps. Yeah, it takes the swelling, it takes the - if you do it straightaway,
679 [yeah] it takes the swelling just that - just down a little bit where I guess it isn't
680 stretching the skin quite so much and not throbbing so much.

681 F: We've got erm gel, cold gel, it's in a [40:01], you put all them round and round his wrist
682 and round his ankle and on the [40:04].

683 M: Yeah, it would cost you a lot of bags of peas wouldn't it for you? Unfortunately.

684 F: You keep on putting in the freezer, [yeah] you know. [right] [right]

685 M: You just have to be careful not to eat the bag of peas [laughs]. [oh yeah]

686 PC: Okay. And so Ray, you said you take a tablet every day but Ron and Eddy, you don't take
687 anything.

688 M: No I take when I have an attack like I take one, sometimes if I take - you feel it coming
689 on and you take it, within a day you can get rid of it.

690 M: Yeah, yeah. If you catch it quick enough.

691 M: Yeah, you know.

692 M: Sometimes you can.

693 M: You can get rid of it within a day, [40:34].

694 F: What tablet is that then?

695 M: I think it's - I don't...

696 M: It's an anti- I take an anti-inflammatory tablet.

697 PC: Naproxin.

698 F: Anti-inflammatory.

699 PC: Naprozin.

700 M: Naprozin. [40:42] a couple of different ones. [40:43] and all that lot, you know so it's -
701 it's just - see if you can catch it it lasts a day but other times it can go on for days and
702 days and if you don't catch right at the start, I think - if you know it's coming on and
703 you've got tablets, you can take it, you can [40:55] but if you leave it a couple of days,
704 and let it settle in a bit and then start taking them [yeah] it takes longer to clear it I
705 think.

706 M: But surely that isn't a treatment for gout, is it? It's not stopping gout.

707 PC: No, no.

708 M: That's a treatment for swelling.

709 F: That's a management.

710 PC: yes, yes. So that's - that's my next sort of erm question to all of you, what do you know
711 about the long term treatment for gout, not just the swelling and the pain aspect,
712 because obviously that's important. But longer term, are you aware of how it's affecting
713 you body or what - why you should have treatment for it on a daily basis?

714 M: I don't - I'm aware that erm my toes are not bending as much as they used to.

715 M: Yeah, mine are...

716 M: And they're a bit painful, yeah?

717 M: Yeah mine do.

718 M: And that to me is a side effect of the gout.

719 M: It is.

720 M: Yeah, yeah.

721 M: My finger, I can't pull that right back. [yeah]

722 M: I get it in my fingers.

723 M: [right] I can't move it like, you know, I can't move it like the other one.

724 PC: Right, okay. So that's...

725 M: And I still get a little bit of pain now and again, outside the gout attack. And I guess
726 that's just arthritis in my toes, I don't know.

727 F: It just affects [42:05] joints then.

728 PC: So you mean in between the acute gout attacks you're [yeah] still getting the pain?
729 [yeah] Right.

730 M: Just a twinge. A twinge.

731 M: It affects all your joints anyway. All the time.

732 PC: Yeah, yeah. So do you know what the long term treatment is for, has anybody explained
733 why you should be on a tablet?

734 M: No.

735 M: No.

736 M: They haven't to me anyway. [no]

737 M: I mean I've looked on the internet again, there's a tablet you can take that you take once
738 a day, and initially it gives you a gout attack, and then you shouldn't get any more after
739 that, but maybe not.

740 PC: And how would that make you feel getting a gout attack from the treatment? Is that
741 bizarre to you?

742 M: Frightened. That's why I never - until recently went to investigate it with the doctor, you
743 know, or ask if I could go on it.

744 PC: So that put you off?

745 M: Yeah, it did, yeah, I mean a bit silly, but yes it did, yeah.

746 F: But it does bring an attack on. Because these tablets that John's had, [42:57] and the
747 Allopurinol, it does initially bring on a bit because we've been going away, and he's
748 having to take it and we thought well, daren't take it.

749 M: [laughs] I daren't take it.

750 F: He daren't take it until we're away and we know we're going to have say two weeks
751 away, and then you can cope with it, for a couple of days and then...

752 M: I can rest.

753 F: ...and then it manages it a little bit.

754 PC: So why do you not take it here, and you take it on holiday?

755 F: Because getting away, he couldn't cope...

756 PC: Oh okay, right.

757 F: ...with getting there.

758 PC: To get the flight and...

759 F: Yeah but once you're there, well we tow a caravan, [as well] and I'd - I drive but I didn't
760 tow the van, so John has to - once we get there, we can set it all up and everything, and
761 then he can relax, put his leg up and put the cold and hot and [yeah] you can manage
762 then a little bit better. But the tablets [right] don't seem to manage it as well.

763 PC: Right, so you - you think managing it with whatever tricks you have on your own is
764 better than the tablet? [yeah] And - so were you expecting that to happen, the attack,
765 when you take the treatment for gout? Or was that...

766 F: Well yes because he was told.

767 PC: You were told about that. Right. Right. Okay. What about anyone else's experience of
768 that? No?

769 M: No.

770 PC: Okay and if you were explained the reasoning behind these longer term treatments,
771 would that make you take it, would you be more inclined to take it then?

772 M: It's difficult, I mean I'd just like to take something, okay, just take one once a day and
773 everything else would be okay, with no side effects, I think I would, you know, as long as
774 it keeps it away. You know...

775 M: I think side - what are the side effects, you know because you've got to make your mind
776 up whether the side effects are worse than what you've got. [yeah, absolutely]

777 F: If somebody was going to say to you...

778 M: All the tablets we take have got side effects haven't they?

779 M: Yeah of course they have.

780 PC: Yeah, yeah. That's true. Yeah.

781 F: But if somebody was going to say to you, if you take - if you don't take this tablet,
782 eventually the gout will overtake it and [yeah] you'll end up with half a leg. I know that's
783 extreme.

784 M: Or in a wheelchair.

785 F: In a wheelchair, yeah. I mean then you'd be prepared to take it.

786 M: Oh aye.

787 M: I mean I'm prepared to take it now...

788 M: Well I take it...I take mine.

789 M: ...and my doctor tells me that the level in my blood, the erm...

790 PC: The uric acid.

791 M: ...is it lactic acid is it?

792 PC: Uric acid.

793 M: Uric acid, erm isn't high enough to warrant it.

794 PC: Okay.

795 M: She thinks the balance isn't, you know, bad enough to deal with it.

796 PC: Yeah, sure.

797 M: Okay, I accept that.

798 PC: And that's another interesting aspect, so if - do you get regular checks from your doctor
799 about your levels of [no] your uric acid in your blood or...?

800 M: No I don't, no.

801 PC: No.

802 F: John does.

803 PC: You do.

804 F: Because...

805 M: I'm at the clinic now so...

806 PC: Because you come to the - right.

807 F: He's been referred to the gout clinic at the Haywood [yeah]. And he goes regularly,
808 yeah. Like he's going on Monday, he's got to have a blood test first, [yeah] and he's -
809 they're going to put him on another tablet, a management tablet [right] that'll sit well
810 with his other tablets.

811 PC: Okay, okay. Yeah.

812 M: I hope anyway. [laughs]

813 M: Well there's a guy comes in erm by us and he was saying he'd lost about four stone in
814 weight, he was [46:19] he had a lump growing out of his elbow here, it was that big like,
815 it was like cricket ball, you know, coming out there. His feet...

816 M: Mine does exactly the same.

817 M: ...and I think it had affected him, he had to go about two years ago he lost about four
818 stone in weight, he was a big bloke, and he just - he's lost all his weight now. And he was
819 on death's door like, you know, and it was - they reckon it was all - because he had a
820 gout attack and he gets it bad, and it affected his heart apparently, like you know I didn't
821 think - you don't ask too much like do you, you know, his wife was you know petrified
822 like I say.

823 F: So it builds up anxiety then doesn't it?

824 M: Yeah, it affected his heart, his gout did and he was in hospital for oh...a good month he
825 was in hospital. I'd go how's Keith? How's Keith? And he was like - he's really ill at the
826 moment and it was all down to gout you know. But he's got over it and he's - I don't
827 know, he still gets bits of attacks, but I think he has to have regular visits to the hospital
828 now to erm...

829 PC: Right, yeah.

830 M: But as I said before, it's still - it ain't looked on as a serious complaint to be honest. [no]
831 [right] You know it's not...

832 PC: Is that something you would prefer, like being you know checked every six months or
833 whatever? Is that something...?

834 M: I think it's - I think gout needs to be, it's only like my view anyway, to be taken more
835 serious because there's more people got it than what you think - than what you realise,
836 you know, [47:43] and they might not get it for five or six [47:42] and forget about it but
837 if you get it regular, and it's the same old thing, gout, if somebody says oh I've got
838 bloody cancer or something, you know what I mean, it's this old - it's this thing
839 erm...they don't realise what it is and they just use the old wives' tale, the port and
840 pheasant, rich living, it's not, you know, and as we said before.

841 M: It's always in the Punch magazine wasn't it? They were always in a bath chair and...

842 M: Yeah and it's like - I think it should be, you know, should probably be a bit more research
843 into it like this which all helps. Something you know more looked into because there's
844 more people got it than like than what you think.

845 PC: So how can we improve that sort of people's perception of what it is? Is there a way
846 round it for a GP?

847 M: I don't know maybe a bit of advertising really like, you know, I mean there's people get it
848 and [48:22] and if you say to somebody I've got gout, they say [48:29] you don't have to
849 eat rich foods and drink a lot. I said you know you don't have to.

850 M: I think erm the other side of it in a way is that erm the - when you've got gout your
851 partner or friend or whatever, if they see you with gout when it's bad, they suddenly
852 realise how bad it is and what it's about. [yeah] You know. But if they haven't seen you

853 with gout, oh you've got gout again, have you? Oh well he'll get...you know, that's it. It's
854 not - it doesn't register as a painful illness.

855 F: That's true because our friends, when you said we've been away, and they've seen him
856 they couldn't believe it, like you say, until you see it. Especially in all the different joints,
857 and like you said a big lump comes up, but John's, touch wood, has always been able to
858 go to somewhere, even if we've been away, and they've drained it off. Because that
859 lump is all fluid and that. And they'll drain it all off.

860 M: Oh it's excruciating pain isn't it?

861 M: Oh aye, absolutely.

862 M: Well they stick needles right through your knee and that to get it out, [yeah].

863 F: But it does - but it does cure it doesn't it? [yeah] But then two days after...

864 M: It takes the pressure away.

865 F: Oh all the pressure's gone.

866 PC: Yeah so you don't mind having it drained and...

867 M: [49:40] to the hospital to get it off.

868 F: I had to get him in a wheelchair because all his left side he can't move at all.

869 PC: Right, right. And that's interesting Eddy, that you've said about the advertising bit, do
870 you mean like on television or radio or...?

871 M: Well anything, just making people more aware of what it actually is really. You know,
872 people need to be [right] made, just as I say people getting it and...

873 M: Because it's just a joke at the moment.

874 M: It is, aye. It's just a joke, you know, ah you've been on a - you've done a bender. Yeah,
875 that's what it is like. You know, oh you've been on a bender, or you've been on - you
876 know, or you've been you know too much rich living and that, I said rich living? You
877 know, I don't. I never have been that - it's not - I don't eat - not eat rich because of gout,
878 because I've never been brought up that way and I've never fancied, you know, the high
879 life and all that. So that is sort of pie in the sky really, it's - I think it's - a lot of it could be
880 hereditary I think. You know, and I could be you know and sort of - and if you do get it,
881 it's being able to watch what you eat really, you know, just a bit of - maybe when they
882 go into clients or the doctors surgery, just to be told and made aware of it, you know
883 [okay] because a hell of a lot of people you hear about it now, just start talking about it,
884 friends and that, and they go oh, it's gout there. And they don't realise.

885 PC: Right, okay.

886 M: The common place is in the toe isn't it like you know. As soon as somebody says they've
887 hurt their foot I said you've got gout you have, you know, I said...

888 PC: And you say that to others do you?

889 M: I say it to anybody, I say if they've hurt their toe, in their toe, I say you've got gout.

890 M: You know if you've got gout. [yeah]

891 M: I say...

892 M: Apparently. [yeah]

893 PC: What - so what would, yeah, if you met someone who was recently diagnosed with
894 gout, what sort of advice would you give them, what would you say to them?

895 M: Keep off their feet, put your feet up.

896 PC: What did you say, Ray, sorry?

897 M: Keep taking the tablets.

898 PC: Keep taking the tablets, right. Okay.

899 M: But I mean just keep your feet up, [yeah] and put a cold compost on, or whatever you
900 call it, a bag of peas, on the foot, stay off of it and erm...take an anti-inflammatory
901 tablet.

902 M: I would say go and see somebody who knows that they're talking about with gout.
903 [yeah]

904 M: But it seems mainly...

905 M: Because most doctors don't.

906 M: It seems mainly the male thought doesn't it? [yeah] I've never heard any women having
907 - I've never heard of a woman, it just seems to be a male thing.

908 PC: You've never heard of women having it?

909 F: There is, we've gone to a - we've been to a couple of other studies here and there are...

910 M: Is it [51:55]? She's got it in her finger.

911 M: I've never like - I know a woman who had gout, but everybody in the hospital I met are
912 all blokes.

913 M: Yes, she got it here in her finger.

914 F: There was three different ladies.

915 M: There, and it swelled up and it burst.

916 PC: How does that make you feel gentlemen, that women - or we think women don't get it?

917 M: They don't have much pain do they? [laughs] They have a softer life than men don't
918 they?

919 PC: Do they?

920 M: Oh steady.

921 PC: All right, you'll get him later. [laughs]

922 M: Maybe some to even up the childbirth thing.

923 PC: Yes.

924 F: Yes but there are a few ladies [yeah] in this group.

925 PC: Yeah, yeah.

926 M: But they don't normally do they?

927 PC: It's less so than men, that's true.

928 M: And you live longer.

929 PC: Yes.

930 M: So what does that tell you?

931 F: That's another subject.

932 M: Just moving sideways from that, I mean just a question if I may ask it, is erm can gout be
933 brought on by stress?

934 PC: It can, yeah.

935 M: I can - I can put some sort of earmarks down on the ground, where stressful times have
936 been. [really?] Erm and you know maybe then I eat something to satisfy that and I have
937 an extra few drinks [yeah], you know, I don't know but I just wondered if it is possible
938 for that?

939 PC: Yeah, no, it is. I don't know what other people's experiences are, but erm...?

940 F: Well John with medical conditions.

941 PC: Yes, so you mean when he's...

942 F: Yes, like the aneurism and he had nodules on the lungs as well and his bypass and all
943 that, that - that was a shock to the system say, and I think that...

944 M: Triggers everything off.

945 F: Triggers things off. [right] And like I say, stress, is it...? [okay]

946 M: I think really, I mean...[53:42] to find it really because if you're - it's going to go into to do
947 more research into it, is get a group of people, [53:49] and give them a 12 month dairy
948 or something like that. [right] And write each day what they've done that day. [okay]
949 What they've drunk that day. What they've eaten that day. [yeah] And do a research
950 programme like that and maybe you could come up with some facts and say well, this,
951 that and the other, or they did have a stressful day at work or whatever, everything they
952 did and...

953 PC: That's a good idea.

954 M: You know what I mean? And then it might give some clues to what - what then - and
955 then if you do get an attack, you'll have had an attack and you can try and map it back a
956 bit and sort of like do an audit trail back and find out [yeah], you might be - it might be
957 that - you don't know do you, you know, you...

958 PC: Do you think people would be acceptable to give out that sort of detail?

959 M: Well if they want to go into a research programme, they have to be don't they? [yeah]
960 You know you're saying this is what you've got to do, and you need people in there who
961 are prepared to do it for like over 12 months, [yeah] and find out and you might come
962 up with some better answers, you know, or lifestyles [right] and whatever they do, you
963 know. It's erm - I think that's the way forward to find out how to do it and you know you
964 could say oh, we had that that day, had a curry that night and the next day, you know,
965 you don't know do you? [no]

966 F: Well one gentleman on one of the study groups, he erm was like that thinking oh what
967 has he said, and he had erm four cans of Guinness, and it - he knew it would bring it on,
968 and - and true as his word, it did, the next day. So there's no way he has Guinness any
969 more.

970 PC: Right, yeah. Yeah.

971 F: I remember him saying.

972 M: [55:12] I had that pint of cider, and I've never touched it since, like you know.

973 PC: Okay. Any sort of other thoughts from any of you about particularly the treatment
974 aspect of gout? Anything that you - like you've said, to you know keep it at bay means a
975 diary of things you can and can't do. Any similar thoughts for the treatment of it or...?

976 M: Not really, no.

977 F: Or you would say that the injections that you're having are more [55:47] sort of thing,
978 after they've had the drain, it does go off a lot quicker than taking the tablet. [right]

979 M: Oh definitely.

980 PC: So the speed of treatment is important I guess?

981 F: Speed, yeah. Yeah.

982 M: Definitely. Yeah. Especially with the injections.

983 PC: Yeah and how do the rest of you feel about that sort of - it's not invasive but fairly, you
984 know, like injection compared to tablet, is that something that puts you off? Or...would
985 that not bother you?

986 M: It's not put me off.

987 M: I think anything that cures it or puts it away, you'll erm - you'll have it, I would like you
988 know. If it can cure it, I'd do I would.

989 M: And the drain is really [56:29].

990 PC: But if it keeps happening, you know...

991 M: It keeps happening.

992 F: Yeah, well...

993 PC: You don't mind doing it again and again?

994 M: No.

995 F: He'd rather not...

996 M: I'd rather not.

997 F: ...and have something that doesn't come on wouldn't you? [yeah]

998 M: I mean sometimes like you know [56:47] somebody says you've been diagnosed with
999 gout, but someone can be diagnosed to an alcoholic or - and it's just you know, but I
1000 think you should be able to be diagnosed you know it's a serious painful - and it does
1001 affect your way of - it affects your way of life, you know, if you get it, you can't go to
1002 work. [no] You know, if you're [57:04] you can't go to work, so it is a serious - it is
1003 something serious, you know.

1004 F: It's got to be taken more seriously.

1005 M: It's not like having, you know, if you get a cold or toothache you can still go to work, if
1006 you get gout in your foot, which is the most common place gout happens in your big toe,
1007 and you're a manual worker, you can't - and somebody says [57:20] you know you can't
1008 go to work on it. And [57:24] obviously times gone, to be diagnosed with gout, like
1009 people can get diagnosed to be - you know, and I think it's more - alcohol is brought on
1010 by yourself, but gout isn't brought on my yourself, it's just your body that's done that.
1011 [57:41] you've done it yourself, basically it's self inflicted, in my opinion anyway. Like
1012 smoking. Self inflicted, but gout isn't self inflicted but then you're diagnosed, you know,
1013 for being an alcoholic, but I think you should be able to be diagnosed to have, you know,
1014 you suffer with gout. So it could actually have a bit more [57:57] held with it and be able
1015 to go and get - rather than me go and wait five days to get to the doctors, to get my
1016 packet of tablets [58:04] you know, be able to go and get my tablets.

1017 PC: And you said, Eddy, that you can't go to work and it affects your life, how have people,
1018 your family, erm you know that - has that had an impact on your relationships with
1019 others?

1020 M: Well no because as I said earlier it's still - gout is still treated as a bit of a joke. Oh you've
1021 been drinking again, ain't you Eddy? You know, I don't drink.

1022 PC: Your family, so you - do you mean...

1023 M: Well I haven't got any family, there's only my sister like, and then like, you know, so -
1024 and she's always off abroad, she was always abroad, so [right] - but her - her ex
1025 husband, he's dead now, he erm - he used to suffer with it as well. [right] He suffered
1026 with it. But as I say it's still treated as a bit of a thing, you know.

1027 M: I think doctors do actually.

1028 M: I think they do, yeah. You know, you've been drinking. How much do you drink?

1029 M: They're not that interested in gout.

1030 M: No, you go in, you go in, you're the doctor, how much do you drink? I said I don't drink
1031 doctor. I said I drink once a week, that's all I do. I said you know my - my sport and
1032 athletics, what I've done in athletics, I said you know how good I was and that, I says so
1033 I'm obviously a fit bloke, he says [59:08] I don't drink like, you know. But they still -
1034 doctors still treat it as a bit of a you know...it's not taken seriously enough.

1035 M: No, no, definitely not.

1036 F: So like partners, have you got a partner or a wife or...?

1037 M: [59:17]

1038 F: Do you think your wife suffers when you've got gout? Does it have an effect on your
1039 wife?

1040 M: Well I lay on the settee with my foot up for a couple of days, and she looks after me. But
1041 she's quite happy to do that.

1042 F: Yes, oh yes.

1043 M: It's not a problem. No. it's not an issue.

1044 M: Pat does with me, but it's quality of life.

1045 F: It's not an issue.

1046 M: Well I live on my own you see, so I've got nobody that can go and make me a drink or
1047 anything like that, I have to do it all myself.

1048 F: Yes, well [59:43].

1049 PC: So you live on your own Ray?

1050 F: So just scream at the wall? Mmm.

1051 M: Yeah I live on my own. The trouble is you...

1052 M: Scream at the wall. [aye?] You scream at the wall.

1053 M: You have to get up to do certain things. [59:51] [yeah] Sorry, you gave to get up and do
1054 certain things yourself, when I know [yeah] as long as I keep weight off the floor, there's
1055 a period of time and it will go away. Whereas if I don't, erm I mean the last attack I had I
1056 think I was in the middle of decorating, so I carried on through once the first day had
1057 gone, and suddenly it all flared up again, and then I realised what I'd done. So you
1058 know...

1059 M: Yeah.

1060 PC: So how do you cope, Ray, if you're on your own and it happens? What - do you just get
1061 on with it?

1062 M: Well I just take the tablets, same as I say. Nothing else.

1063 PC: Yeah, yeah.

1064 F: And you hobble about do you?

1065 M: I hobble about, aye, you've got to haven't you?

1066 F: You've got to. Yeah.

1067 M: You have to aye, you've got to...

1068 F: Yeah, because you're on your own.

1069 M: It's not going - you know, you've still got to [60:36] make yourself a drink and go to
1070 work, you know.

1071 M: [60:36] feeling sorry for yourself. [no] You know, you've still got to go to work and all
1072 that. You know. [right] [60:42] erm what they call them, them crop things with a big
1073 white thing you see [yeah] I stick them on and go to work in that, gout [60:52] do you
1074 know what I mean? Don't come in at all but...

1075 PC: Yeah, yeah. And are your workplace sympathetic, [no] do they...?

1076 M: No, no, nobody's sympathetic about gout. [no?] No.

1077 F: Because they don't take it as a serious complaint.

1078 M: If they don't know - if they don't - they don't think it's serious, people at work, people
1079 that work anywhere you go, you know you say - they take it seriously, it's not taken
1080 seriously, they don't take it seriously do they? They just think oh, you've got gout, oh
1081 don't worry.

1082 PC: So they don't sort of say okay, have time off or sit down and do...?

1083 M: No, [61:20].

1084 M: No, think it's like - it's like having a cold or a bout of the flu or something.

1085 M: [61:25] to the gym many times and they'll say I'm afraid it's gout, gout? And just laugh at
1086 you. [yeah]

1087 PC: Right, right, yeah.

1088 M: Yeah it needs some, you know, it's like I say I don't know, just make people more aware
1089 of - because it could happen to anybody, we all know, and [yeah] it seems to be
1090 happening more and more. You know. Happening just - [61:45] put posters in doctors...

1091 M: But why, why is it happening more and more?

1092 M: I think - I think - I think our lifestyles are changing. You know, we're...

1093 M: 50 years ago, you know, you didn't hear of it. In Punch, you used to get it in Punch,
1094 somebody in a bath chair and [yeah] you know with a big bandage round his foot and
1095 [yeah] that's all you ever heard of. [yeah] You never heard of gout.

1096 M: Yeah I mean our life - all our lifestyles have gone up [yeah] and become much more erm
1097 trying different sorts of foods more often when you like them. [yeah] I mean once upon
1098 a time you only had chicken on Christmas day, now it's everyday of the week sort of
1099 thing.

1100 F: Now you have it every week.

1101 M: You do? [yeah] [62:25] [laughs]

1102 F: Yeah so you want more media coverage, that's what you're saying don't you?

1103 M: Well I think you just see them when you go in surgeries, do you know what I mean?
1104 [yeah] Just sort of, you know, a poster or something like that [yeah] that says well do
1105 you know what gout is, a lot of people don't realise you know what it is, that's [62:40] it
1106 could be in the research, you know. And it's just, you know, it's - you get - after a bit you
1107 get fed up of the old pun of saying, oh rich living that is, you know. [62:48] rich living.

1108 F: So perhaps in GPs surgeries when you go and the wall is full of all these - you'd like one
1109 for gout?

1110 M: Mmm, that's it, everything else don't they, you know.

1111 F: Gout is a serious condition.

1112 M: Well it is isn't it, you know. If you...

1113 PC: You mean where the leaflets are about [yeah] you know smoking or whatever, and...

1114 M: Yeah. I mean you go to work and they say oh this, and they have this, that and the other,
1115 you know, and you're asking them to come to work, you're asking them to do these jobs,
1116 but people don't realise what it is. They don't realise what gout is and the effects it can
1117 be and where it all comes from, you know, and sort of - it is your blood basically isn't it,
1118 do you know what I mean? It's a problem in your blood and...

1119 M: But why [63:24] why the change?

1120 M: Well I put it down to the feeds they're giving these animals I do. Because they hadn't
1121 used to feed them with tablets same as they do now. It used to be all slops and
1122 everything. And it tasted better, the food did. Years ago, than what it does now.

1123 PC: Okay.

1124 F: So do you think it's more a chemical?

1125 M: Yeah it's chemicals.

1126 M: I put mine down to my tablets that I take, like [63:53] tablets that I take.

1127 PC: You think it's down to that?

1128 M: Aye.

1129 PC: But were you diagnosed before you started taking those tablets or did it happen after?
1130 With gout I mean.

1131 M: After, after.

1132 PC: After, okay. Yeah. Yeah. Do you...yeah...

1133 M: I mean I like fruit, I love fruit, but I keep off it so much now because of the acidity in it like,
1134 you know, I mean...

1135 M: Well I've been told I can eat anything. [yeah]

1136 M: Yeah, fruit's all right is it?

1137 F: Yeah.

1138 M: Yeah, fruit's all right. Pickled onions are all right. Cabbages.

1139 F: As long as you're not having it all the time.

1140 M: Yeah.

1141 PC: It's all...

1142 M: Do you think it is meat then?

1143 M: I kept off all that, I just kept off meat.

1144 M: Mmm, do you think it is meat? Do you think it is?

1145 M: I don't know. That's what I'm struggling to - I don't know. In all honesty.

1146 PC: Is it hard for all of you to - to have all these conflicting or different advice, you know, you
1147 hear from your mates, you can eat this or you say you can't eat that, [yeah] so how do
1148 you decide? What do you do?

1149 M: Well I've just made...

1150 F: You've got to do it yourself.

1151 M: ...made a - I looked, thought about it, made my own decision, and I just stick by my own
1152 little rules. And it seems to...[right] my gout is better than it used to be [yeah] for one
1153 reason or another, whether I'm managing better.

1154 F: Because you go on the internet don't you and there's different, conflicting things on the
1155 internet even.

1156 M: You have to take all that with a pinch of salt.

1157 M: Well I think the same as Ron, [yeah] I do - I try and cut out things and keep away from
1158 things. But then again...

1159 M: I wouldn't say I cut things out, [no] I just eat - make sure I eat less of them [moderation]
1160 and don't eat them so often. I still enjoy things that I shouldn't have, you know like a
1161 pint of Guinness for instance. [do you?] Yeah. But only once a month. You know, not
1162 three or four times a week. [no] You know. That's the difference.

1163 PC: Right.

1164 M: I think that's what it is, it's - it's managing it and having not as much, [yeah] all the time.

1165 M: Well having your life as you - as you want it. You know, you're going to make yourself
1166 really miserable if you cut everything you shouldn't do [yeah] in life.

1167 PC: And so Pat, specifically for you, from a partner's [right, okay] family perspective, what do
1168 you wish for gout, or it's treatment, to be like and you know have you any sort of
1169 thoughts about it?

1170 F: A bit more instant, from a flare up, [yeah] most definitely. Because the pain can really,
1171 really excruciating pain, it can be the whole day or at least ten hours, and it's - at night
1172 times is worse, and you can't do anything, there's - no matter what you suggest or what
1173 you try to help, whether it's elevate the leg or put the cold on, put the hot on, and
1174 erm...it doesn't seem to have any effect. Not in the instant, first instant, then
1175 afterwards, yeah, you can lie on the settee for the next couple of days and then take him
1176 food and help him go to the loo and things like that.

1177 PC: And how do you feel about all of that, sort of taking care of him?

1178 F: Well it's part - part of being married really.

1179 PC: Yeah, right.

1180 F: You get on with it don't you, like you know. But the quality of life isn't there is it? [okay]
1181 You know, so it's erm - it does get frustrating because...

1182 M: I think what annoys me is I mean sort of on a political point of view, is sort of this is not -
1183 it's a problem we've got with our health and that, it's not - whereas they seem to put
1184 more emphasis on research on self infliction.

1185 F: Yes, like if it was drugs or...alcohol.

1186 M: Like you use drugs, you know, you see posters everywhere, you know, drugs and that,
1187 but - and alcoholism, that's self infliction. Gout is not self infliction, gout is a health
1188 problem.

1189 M: And yet they spend no money on it.

1190 M: Exactly, they...

1191 M: And don't you feel, sorry, just to interrupt, sorry, people think that gout is self inflicted.

1192 M: Well yeah, yeah.

1193 F: Yes, they do.

1194 M: Yes they do.

1195 M: [67:37] But they'll spend money on erm you know like research and have all these chat
1196 shows of I was a drug dealer, I took drugs and I was an alcoholic, you know. But you
1197 know it's taking drugs and smoking it's self infliction in my opinion. But gout isn't, yet do
1198 you know what I mean? It's - it's...

1199 F: Your metabolism.

1200 M: Yes, it can do.

1201 M: It's your body like, do you know what I mean? And - but they'll spend millions on self
1202 infliction and people taking drugs and all that. [yeah] and I remember when my mum
1203 was in hospital, and they rushed, there was a bloke he'd overdosed in the hospital, and
1204 my mum had had a stroke, and they spent more time looking after this bloke who'd
1205 overdosed on drugs than my mum. So I flared up like, do you know what I mean? I went
1206 - and I'm against - you know so I think there's more - they should spend more money on
1207 stuff which we ain't brought this on ourselves, [yeah] it's because it's an illness, it's -
1208 whatever it is, we've got with us, whereas drugs and - they'll spend money. You see
1209 posters everywhere.

1210 F: Is it classed as a disease of say the joints or the blood?

1211 PC: Erm well it is a disease of the joints but it's a lot more than that actually. It doesn't just
1212 affect your joints as you've all maybe touched upon, because it does affect your kidneys
1213 and your heart and so on. [yeah] And it is related to other conditions as well, so it's not
1214 just joints really. Erm yeah...but...

1215 F: Because of the one tablets that - erm the management tablet, you take one a day, that
1216 erm the GP prescribed for John, [69:07] erm when we went up eventually to the clinic
1217 straightaway oh no, you can't be on that because your history of his heart, you can't
1218 take that tablet. Because there'd been research done at NICE, that said there's no way.
1219 But our GP had prescribed it for him. [yeah] You know so you...

1220 M: But they don't spend enough money on it at all, on gout.

1221 PC: They don't spend?

1222 M: No. they spend more on morning sickness than they spend on gout. [laughs]

1223 PC: We've all heard about that recently. [laughs]

1224 F: He isn't a royalist.

1225 M: I'm not, no. it's just a point that they do spend more money on than they do on gout.
1226 [yeah]

1227 F: Well like Eddy's been saying about...

1228 PC: Yeah, so you wished that they'd sort of advertised more or sort of spend more on
1229 campaigning about gout rather than you know...[yeah] okay, okay, that's interesting.
1230 Okay, erm...anything else that anyone wants to add from your perspective Pat, from a
1231 family's perspective?

1232 F: Well a long term, definitely it needs something long term.

1233 M: Just want a better quality of life, really.

1234 F: Well you get on with it don't you, that's your - you know, your partner's and you get on
1235 with it, you do what you've got to do. Like Ray is on his own and Eddy, they have to do
1236 things for themselves don't they like, you know, so erm...

1237 PC: And does it affect your quality of life?

1238 F: Well obviously, mmm.

1239 PC: In what way?

1240 F: Well we can't go out and do the same things, I could go out and leave him. [right, yeah]
1241 But there's no way I would. [okay] So it does have an effect on the whole unit, even if
1242 you were young and you'd got children and all that like, you know, it would have an
1243 effect on the whole of the household.

1244 PC: Okay, and any final thoughts from the rest of you? Anything you want to add that you
1245 wanted to be put across?

1246 M: No.

1247 M: No.

1248 M: Just like a cure.

1249 PC: Like a cure? Okay. Yeah. [yeah]

1250 M: And a cup of coffee. [laughs]

1251 PC: Sure, I think we can manage that. [laughs] Okay, well shall we sort of draw to an end
1252 then, and erm...yeah, everyone happy with what's...?

1253 F: And what is going - from the research point of view, do - we believe that erm the
1254 arthritis say, erm research team have been given so much money to research into it, will
1255 that include - that'll include the gout and that? So long term do you hope that there will
1256 be a tablet?

1257 PC: Yeah well - yes, it will - yes. Erm...

1258 F: But will it be just erm...like an anti-inflammatory, or will it be a management or will it be
1259 a cure?

1260 PC: Well there are - there are already sort of newer treatments for gout, and a lot of those
1261 treatments haven't come into clinical practice because they're still in the trial phase.
1262 Erm and they are longer term management as well as the you know sort of acute
1263 inflammation sorting out that aspect. So there are already newer tablets. And the erm
1264 money that the government does provide for arthritis overall, particularly here, is you
1265 know heavily involved in research into gout as well and that's why we're doing this study
1266 really.

1267 M: I mean arthritis is a big thing in this country isn't it? [yeah] You know I mean...

1268 M: It's huge.

1269 M: And you don't hear of it in Spain and Italy and Greece do you? You know it just seems to
1270 be [no] this country like, you know, it's obviously the damp conditions isn't, do you know
1271 what I mean?

1272 PC: It's the weather.

1273 M: The weather, yeah.

1274 M: But the doctors erm dad's got it hasn't he? Gout?

1275 PC: Yeah, yeah.

1276 M: Has he? Yeah.

1277 PC: Yeah. Right, so I'll just shut these off and then we can have a coffee.

1 **Focus group transcript 4**

2

3 PC: = MODERATOR

4 M: = MALE PARTICIPANT

5 F: = FEMALE PARTICIPANT

6

7 PC: Okay, so try and forget about that. So, yeah, welcome again and, as I said, the purpose
8 is really just to have a chat about your experiences of the - mainly the treatment of gout,
9 but obviously anything that's important to you about you having gout is also very
10 relevant. So, you know, let, let's get started. I think, Bill, you had good examples of how
11 you came about starting treatment.

12 M: Yes, yes. I mean I start, probably like most of you, with very painful toe joints and the
13 doctor right away said it was gout, you know. I had blood tests, and they said it's gout.
14 Build up of uric acid. And erm I, I was given anti-inflammatories, which, which did the
15 trick. Over a couple of weeks it settled down. [okay] But then a couple of months later
16 it came back again and I went through the same procedure for about 18 months. And,
17 as far as I was concerned, it was doing the job. It was only when erm I found out that
18 my kidneys were being affected that erm the specialist said it was down to taking anti-
19 inflammatories for too long. And I thought, 'Well, what other way have I got?'

20 PC: So when you first got diagnosed, you were just given these anti[-inflammatory tablets
21 [yeah] and nothing else.

22 M: Yeah, nothing else.

23 PC: And how long were you on those for?

24 M: I'd say it was about 18 months.

25 PC: Right. And during that time, how many attacks were you getting, roughly?

26 M: I, I was getting every, every couple of months, two to three months.

27 PC: Right, okay. And has anyone had similar experiences where they've just been treated
28 with an anti-inflammatory or ...?

29 M: I wasn't treated with an anti-inflammatory the first time I went to the hospital. They
30 thought it was erm err arthritis. [yeah] Erm I - they said, 'Just give him painkillers.' Err I
31 had another attack on the other ankle about two, three months later and then they
32 decided it wasn't septic arthritis, it was gout. [okay] So I had painkillers, nothing else.
33 And then I had err three or four attacks since, and after the third one I went to see the
34 doctor and he gave me erm col ...

35 M: Colchicine.

36 M: Colchicine, yeah. [huh-huh] I had them and when I had that attack, after - when I saw
 37 him, four days it cleared up and, touch wood, I haven't had another turn, and that was
 38 in May.

39 PC: Right, okay. So you think those tablets worked well for you.

40 M: Well, up to now it has, certainly for me. He said only take them when needed, when
 41 you get an attack.

42 PC: And how many attacks have you had so far?

43 M: Since I've used those?

44 PC: Well, since you've been diagnosed.

45 M: Erm six.

46 PC: And that's over how long?

47 M: 18 months.

48 PC: Okay.

49 M: As I said earlier, I feel a bit of a sham because I don't seem to suffer from it very much. I
 50 think it was three or four years ago I had my first attack of gout. Erm I was pretty sure I
 51 knew what it was. It was the right big toe joint getting very hot, [okay] very, very
 52 sensitive to touch. Went to the GP, who was very helpful and gave me naproxen, [yeah]
 53 500 milligrams. [yeah] Erm said take two immediately and within three days everything
 54 had gone. [right] I've only had one other attack since then, and that was about nine,
 55 ten months ago. [okay] Erm and I've followed the same regime. Although the dosage
 56 says one twice a day, I take two initially and then one a day, and it's cleared up within
 57 three days. [right] I have erm - even in that attack, it wasn't - I wasn't disabled in any
 58 way. I could still get my shoe on. I could still walk about. [huh-huh] Erm so it's quite
 59 mild and very quickly treated.

60 PC: Huh-huh. You said, Ian, that erm you knew what it was when you got it. How did you
 61 know that? Have you had previous experience of gout?

62 M: Erm well, it, you know, it's about the swollen [04:31], very, very painful toe joints. You -
 63 somebody was mentioning the cartoon earlier on with, you know, the big bandage on
 64 the foot, and I, I just assumed that's what it was. I, I wasn't absolutely certain. Err so I
 65 just went to my GP. [yeah] Erm she err didn't take any blood samples or anything. She,
 66 she agreed that that was it. Erm she did explain precisely what she thought it was. Err
 67 and the practice I go to has two or three GPs and I've always found them very good in
 68 terms of explaining what it is and what the treatment's meant to do. [yeah] And it does
 69 tend to work on err prescribing for what they think it is rather than lots of blood tests,
 70 and if it works, then they were right, and if it doesn't work, then, 'Come back in a few
 71 days.' [yeah] Erm I have to say generally they're, they're right, and certainly with the
 72 gout. They were absolutely spot on.

73 PC: Okay. So you've never had any blood tests for it. Never. Okay.

74 M: No. I occasionally, very occasionally, get what I think of as a ghost attack where I think
75 gout is going to start, but next day it's gone again. So I don't know whether it can self-
76 correct quite quickly. I don't take any medication for it. [right] And in the three or four
77 years I've had possibly two occasions where I've thought, 'Oh, the gout's starting again,'
78 erm it never came to anything. And that's down to really just sensitivity in the, the big
79 toe joint. [okay] And 24 hours later it had, had dissipated, or gone, or ...

80 PC: Right. And do others find it similar, that it sort of happens very quickly and goes away
81 quickly? That sort of ...

82 M: Mine never goes away.

83 PC: How do you mean?

84 M: It's always, always there. I can feel it all the time. It's - err me toe now is throbbing
85 away, you know, [right] toe, big toe. [right] But it will, you know, I, I'm just hoping it will
86 go down.

87 PC: Okay. And what do you take for it, then?

88 M: I take 100 ml of anti-inflammatory twice a day, but where - originally they put me on
89 100 when they fetched me back to the surgery, they put me on 100 ml. And then I had a
90 terrible attack, I was in bed for three days, [right] and I went back to him and told him
91 what was going on, so they just doubled the dose; [right] one in the morning, one at
92 night.

93 PC: And what tablet is it, do you remember?

94 M: I, I don't know.

95 PC: Allopurinol?

96 M: Pardon?

97 PC: Allopurinol?

98 M: I think it is, that. [okay] It was ...

99 M: Anti-inflammatory, did you say? [yeah] That is an anti-inflammatory.

100 PC: Yeah, yeah.

101 M: Erm but, at the same time, they give me the 300 one for a ten-day course. [right] I
102 suppose that's [07:31] the crystal. [okay] Then I went back onto the err the double
103 dose: the 100 in the morning and the 100 at night.

104 PC: Right, okay. Okay. And that's the anti-inflammatory.

105 M: Well, it's there all - I get it in my shoulders. Now, I can feel it now. [right, okay] I sleep
106 on the left-hand side and you have to pack the pillow up and take the pressure there,
107 and then the shoulder's [07:57] [right] go to sleep.

108 PC: Okay. So when, when you were all sort of given tablets, were you explained the
109 different types of tablets [no] that there are? No?

110 M: See, I mean, I mean, he just said, he's talking about anti-inflammatories. Now, to me
111 now, anti-inflammatories isn't the cure. Anti-inflammatories brings it down and
112 eventually your blood gets flowing again. [yeah] Well, it doesn't, as far as I was
113 concerned, with, with having the trouble I had, it isn't a cure, and that can, that can
114 affect your kidneys. [yeah] But they don't sort of follow it up by keeping an eye on
115 whether it is affecting your kidneys or not. [right] That, that's, that's what I, I was trying
116 to say. [right] I think we've all got ignorance of it. Doctors don't sort of explain exactly
117 what it is and what anti-inflammatories do and things like that ...

118 PC: So you perhaps ...

119 M: ... you know.

120 PC: ... like that explanation is ...

121 M: I mean I, I don't know whether I'm wrong or not, but I think allopurinol now - allopurinol
122 isn't an anti-inflammatory; it's support to stop you from producing uric acid, [yeah]
123 which is the ultimate what you want to do to stop gout, is to stop producing uric acid,
124 what your body's producing.

125 PC: So how do you know about that, Bill? Who told you about the ...

126 M: Well, I, I - it was information I got in hospital.

127 PC: Right, so someone told you ...

128 M: From Haywood Hospital, yes.

129 PC: Okay, okay.

130 M: You know, rightly or wrongly. I don't know if it's right, but ...

131 PC: No, it's right.

132 M: ... it's what I understand, [yeah] you know, and that's why I'm always, always erm - I, I
133 don't like taking too many anti-inflammatories now, [yeah] for the sake of it. I don't
134 take them unless I've got to, [yeah] because of the bad experience with it.

135 PC: Right. So how do you manage when you get err acute sort of flare of gout, and what do
136 you take?

137 M: Well, if I get a flare of, of gout, I, I stop taking the allopurinol and I'll take the cortisone
138 tablets.

139 PC: You stop taking the allopurinol.

140 M: Yeah, because you aren't supposed to take the two at the same time, because
141 allopurinol can aggravate it. If you, [right] if you, if you've got a flare up, allopurinol, I
142 was told, could aggravate it. [right] So I was told you had to stop taking that while
143 you're taking your colchicines. [okay] That takes two or three days to settle it down.

144 PC: Okay. And who told you that?

145 M: Hospital.

146 PC: At the hospital. Right, okay. And what about you, the other gentleman?

147 M: No, I wasn't told anything about err anti-inflammatories, erm just painkillers, [right]
148 keep the leg raised, rest.

149 PC: Okay. So you're not on any err long-term treatment?

150 M: No, it's just the tablets [10:37]. [okay]

151 M: See, that, that's another thing, like he says about rest, [yeah] [10:41] should rest it. It's
152 more painful if you rest [right] than not, because it - you're not, not moving at all and
153 your blood's not moving. I mean I used to make myself - I walked with a stick. I mean I
154 played, I play golf, I even played golf with it. I cut the inside of my shoe out because I
155 couldn't get it on; it was that swelled. But I didn't let it stop me from playing golf. It was
156 painful, but, you know, but people don't realise when they say, when they say rest it, it
157 stays in one place and gives you more pain.

158 PC: Okay. So how else, apart from, you know, the tablets that doctors give you, do you treat
159 it? Are there, are there other things that you do by yourself that makes it better? Or
160 have you tried things that have made it worse?

161 M: I, I - to be honest, I don't treat it. [okay] Life goes on and then if I get this ghost, as I
162 describe it, the ghost pain or I get a flare up, I just hit these tablets, five of them sees it
163 off. And erm life just goes on. The only concession I made, and it was the very first
164 attack I had, was I had to wear a sandal on my right foot because I couldn't, I couldn't
165 get my foot into my shoe. [right] But it didn't stop me getting out and about. I just
166 walked about with one shoe, shoe on one foot and a sandal on the other foot, [right]
167 because it was winter. [okay] If it was summer I'd have just gone about in a pair of
168 sandals. [okay] But erm [yeah] I, I don't, I don't avoid things, I don't manage my diet at
169 all to avoid it. [no] I drink the things I like to drink. [okay] Erm, you know ...

170 M: I think food is a, a grey area with it, isn't it?

171 PC: It is, yeah.

172 M: Talk to different people and it's funny how different foods. [yeah] And some people
173 say, 'Oh, not acidic food,' but it isn't necessarily acidic food.

174 PC: We'll, we'll talk about food in a second, Bill. Let me just welcome erm ...

175 M: Robin.

176 PC: ... Robin.

177 M: I haven't got one of these badges.

178 PC: I will give you one. I'm so sorry you've been stuck in traffic.

179 M: No, no, no, I was ...

180 PC: You've not missed much, Robin, because we've just started, what, maybe ten minutes
181 ago, less than that. Erm would you like a cup of tea or coffee?

182 M: Tea, with one sugar, please.

183 PC: And biscuits there.

184 M: And milk, please. Strong, if possible.

185 PC: Would you do me a favour, just pass me those sheets from over there? Thank you very
186 much. So I've explained to the other gentlemen that err what the interview's about.
187 [yeah] You can sign the consent later, if you want. [all right] But, essentially, you know,
188 it's really just talking about your experience of the treatment of gout and how that
189 affects your life, really.

190 M: Can I [13:38]?

191 PC: Of course you can. [yeah] Erm and erm, you know, it's - I was saying to the others that
192 it's part of a larger study and erm if at any point you don't want your quotations to be
193 used or if you want to stop the interview, just say. It's all very informal. Erm and erm,
194 you know, we'll get cracking and then if you have any questions, please ask me, by all
195 means, at the end. [sure] If, if that's all ...

196 M: I'll come over very fluey.

197 PC: And erm I don't know if you've had a chance to read those, what we sent to you in the
198 post ...

199 M: I have read it, yes.

200 PC: Okay. So yes, erm we, we'll give Robin just a minute to, to get settled in and then we'll
201 start ...

202 M: Thank you very much.

203 PC: ... chatting. So the other chaps just erm - the other chaps were just saying about how
204 they got diagnosed and what sort of treatment they were initially put on and, and then
205 we've just approached the topic of what they do and ...

206 M: [14:40]

207 PC: I think erm Bill was about to start about what sort of food, so we'll start that and we'll
208 come back to you about [right] - we'll give you a minute to settle in [sure] and then we'll
209 come back to you. So go on, Bill ...

210 M: I mean, I mean food with me is there's certain things [yeah] that I can't touch at all.
211 [okay] If I've touched tomatoes then within two days I can't walk. [really] It's as simple
212 as that. [okay] You know, it flares up and - but I've got to the stage now where with
213 allopurinol I, I expect that to work - well, it does work all the time. It stops me from
214 producing - and now and then I'll get a flare up and straightaway I, I start thinking what
215 I've ate within the past three days, [right] different. And each time I can think, 'Oh, I've
216 had that different.'

217 PC: So you can spot ...

218 M: So I don't, I don't take - have that again. [right] Some, some people say potatoes affect
219 them. [right] It's never affected me.

220 PC: So tomatoes and what else?

221 M: It's very rare in strawberries. [right, okay] Strawberries. This particular once I was on
222 holiday this year and erm I, I had a flare up and I was with grandkids in the caravan and I
223 was trying to think what I had eaten and erm I thought of such and such a thing and
224 then it started flaring up the next day. And then I found out that we'd have a jar of
225 piccalilli, [right] a different one that I'd never had before, and there must have been
226 something in that [right] that caused it. So I didn't have that. And in two or three days it
227 had gone again. But foods, it's just marvellous how they can set it off.

228 PC: So you've been lucky, then, because you've not had to make any sacrifices in that
229 respect. [no] Err what about other people? Have they found food to be ...

230 M: We don't know, do we, really.

231 PC: How do you mean?

232 M: If you've just eaten what's prepared, what the wife prepares, you eat it, [yeah] but you
233 think to yourself - such as cherries, we're told, are very good for you, aren't they? You
234 get all this sort of thing and you don't know. Dark wine you can drink, but you can't
235 drink erm anything other than dark wine. [right] Is that true? Is that a myth?

236 M: It doesn't seem to affect me because I love red wine and I, I drink more port than I
237 should do occasionally. [laughter] It triggers, supposedly, but I don't know if it's true.

238 M: I mean [17:147], this is what I said on the phone to you. If we can have a sheet what
239 you can eat, [okay] than what you - instead of what you can't. I mean if you could make
240 up err menus of what you can eat, knowing - but there again, what I do now, which is ...

241 M: It's a different thing. But the thing is, when you're getting an attack, it might be that
242 you've ate something, you know. You might just think, [yeah] 'Oh, it's an attack of gout,'
243 but - well, like with me tomatoes, it, it might be that you've ate something like tomatoes
244 and it's starting your gout off, and if you knew that it was that, or [17:51] that, you
245 might not get it err the same.

246 M: Can I just say that erm one can talk personally, and then we can talk in a more general
247 sense, err I mean personally food, food isn't [18:06]. [right] Erm except - I mean you
248 mentioned cherries. Some - I mean my experience appears to be different from yours,
249 but you mentioned cherries. Err some months ago when I had gout badly erm someone
250 did suggest that I - erm somebody involved in health work, that I have concentrated
251 cherry juice, which you can buy, at great expense, from health food shops, and it's
252 delicious. But whether it does it any good or not, I've no idea. But it's nice stuff. [hmm]
253 But I have heard that cherries are good for it. However, erm I believe that there are
254 certain foods that are not good - I'm not talking about me, but in general - for gout. And
255 shellfish is apparently one of them. [hmm] Now, I can only speak - I don't know how
256 long you people have had gout, but erm I've had it and I've now not got it. [okay]
257 Right? Sorry, I still have to take a pill, or at least I'm told I have to take a pill every day.
258 But the gout has gone, for various reasons.

259 PC: So let's, let's - because we missed your sort of [yeah] background, Robin, [yeah] so tell
260 us a bit about ...

261 M: How it started?

262 PC: Yeah, and err how long you've had it for [yeah] and ...

263 M: And why it's gone.

264 PC: Yeah, and, and who told you about taking - carrying on with the pills and - yeah.

265 M: Well, erm if you're going to the history, I used to - I have been a teacher for the past err
266 30 years and I've just more or less retired erm in the summer. And I used to work for
267 many years in London, which is where I'm from, and until - well, until 1998 err when I got
268 early retirement from a job in the East End of London at the age of 50, erm I used to
269 cycle every day everywhere in London. And most of London is flat. And I would do 20 or
270 30 miles every day and although I used to drink quite a lot at the end of the day, like
271 most teachers, I was fit as a fiddle. And then what happened is this. Erm because I'd got
272 early retirement, that's long story, but err with - after about four months of not cycling
273 every day, although I still cycled sometimes, I suddenly woke up one morning in October
274 1998 and err I got out of bed and appeared to have broken my ankle overnight. I
275 thought, 'I haven't broken my ankle,' you know. I hadn't fallen down or nothing. So I
276 went to see the doctor, whose name, as I say, was mine, oddly enough, and she said,
277 'Well, you appear to have got gout.' [huh-huh] And I thought, 'Eh? I haven't been in the
278 trenches,' or all those other myths about gout, drinking port, which I've barely touched
279 in my life. And she, she said, 'Well, one in 1,100 people get gout and erm it's a genetic
280 condition and,' she said, 'Nothing to do with what you eat or drink. You've got it, chum.
281 You're one of the one in 1,100.'

282 PC: Can I ...

283 M: Sorry, yeah, go on.

284 PC: Can I ask you about - all of you about the myths, then, because you've raised [yeah] sort
285 of the myths about gout. Apart from what you've said, what, what has everyone heard,
286 heard about, you know, sort of the, as you said ...

287 M: Well, I think there are a lot of myths, you know. It, it used to be considered err the
288 result of eating too much rich food and drink. [yes] Erm I never gave any credence to
289 that because my sister in law's first husband, who lives a very frugal life in terms of the
290 quality of food and drink, err suffers significantly with gout. [yeah] And I think because
291 people don't really know why it happens - they know what causes it, you know, the uric
292 acid crystallising out of the joints, but what causes it, I think, is still a bit of a mystery.

293 M: Can I say a bit about that?

294 PC: Yes.

295 M: Erm err I've been a history teacher and I'm still involved in historical research. I haven't
296 done any research into gout because I've got other things to do, as it were. However, I
297 spoke - following on from your point, I spoke to my old history tutor, who's now 79, he
298 said, 'Well, it's a disease of the aristocracy and erm, you know, from the 18th century.'
299 And well, I said, 'Okay, but it's bloody painful.' Erm and - well, I, I don't know enough

300 about it, but it is said to have been from eating and drinking too much, and if you read
301 people's diets from 200 years ago it's not surprising. [hmm] But I mean - and it is
302 primarily connected - someone has said it is connected with port being imported from
303 Portugal in lead-lined barrels, but I don't know. Have you come across that?

304 PC: Yes, I have.

305 M: Yeah, well lead is very bad for you, [hmm] however it gets into your system. So that's
306 one - that's one myth that [okay] might have something to do with it. I mean I don't
307 know whether I should just go on about what happened. She, [yeah] the doctor, said,
308 'You've got gout.' Err I thought I had a broken ankle. And she said, 'You - when you get
309 gout you take one of these tablets,' indometicin, [right] and they're very strong. Do any
310 of you take them?

311 M: Oh, they are, yeah.

312 M: Yeah. But they're very strong and she said, 'Well, you mustn't take these for long
313 because you might get stomach ulcers.' And I thought, 'I don't want any of them.' 'So
314 you take - what happens is you take them and it goes away,' and it went away, quite
315 quickly. It's almost like a miracle cure, within about 24 hours of taking them.

316 M: What are they?

317 M: Indometicin.

318 PC: Anti-inflammatory ...

319 M: Indometicin?

320 M: Yes. But don't take - you, you've got to be careful with them, because if you take them
321 for any length of time, you'll get worse things, so they say. So anyway, so from '98 until
322 last autumn, I would get gout every so often.

323 PC: How often?

324 M: Well, I haven't kept a diary. That's not true, I have kept a diary but I haven't got it with
325 me. But, let's say, once a year. [okay] Excuse me, and you take a pill and it went away,
326 and sometimes you had to take three or four days' worth, and sometimes it's worse or
327 better, etc. Well, what happened then is that, let me think, I must have had gout quite
328 badly all of - nearly all of last summer, not, not this one, the one before. I was in the
329 South of France and I could barely walk. I was taking - anyway, I went back to work and,
330 in fact, all through the winter term last year erm I had gout and then suddenly it got so
331 bad it was terrible, [huh-huh] in November 2011. And erm I went to the doctor and she
332 said, 'Well,' she said, 'You're going to have to change your medicines. You're going to
333 have to go on allopurinol every day.' But in the - in this kind of in-between period, I
334 don't know that he warned me about this, but you're likely to get a very severe attack of
335 gout, which is what actually happened. [yeah] And by the end of the winter term I was
336 in the most excruciating pain. I mean I haven't borne any children, but my long-time
337 partner - I mean it must be just as bad as childbirth. I believe it is, anyway. And having
338 almost never taken time off work for about 40 years, I suddenly had to have the whole
339 of January off and unbelievable pain.

340 PC: Was that - what were you saying?

341 M: Unbelievable pain. [yes] Well, I mean is it all right if I just go on?

342 M: I'm leaving at 1 o'clock.

343 M: I don't intend talking that long. Erm well, by this - as I say, I had the whole of January off
344 work, but I didn't even know how to write a sick note. So, strangely enough, I live in erm
345 Ironbridge and my local pub's called The Coalbrookdale Arms and there was me and this
346 other bloke in there one evening and he'd broken his leg very badly in a car crash. So
347 we were both in there, almost like a kind of hospital ward, having a pint. And he
348 happens to be a psychotherapist. And we were talking about our pain, and he said,
349 'Well, do you remember how the, the - what brought it on in the first place, i.e. 13 years
350 ago? Was there some kind of change in your routine?' And, of course, there had been a
351 change in my routine which was that I stopped taking erm serious exercise err and -
352 well, what happened gradually is that I gradually took less and less exercise and I put on
353 weight and all the rest of it. Erm and I, I now discovered, through talking to one or two
354 other people, I've only got a small sample, but this was their experience as well. Having
355 done jobs - a gamekeeper, for instance, who used to walk, you know, miles and miles
356 every day and then suddenly he retired and he had gout, almost within weeks. [right]
357 And his wife said, you know, 'Can't do anything about it.' But I mean the exercise has
358 been - because I've now got reasonably fit over the last few months and I've lost a bit of
359 weight, although you've really got to do serious things to lose weight seriously and
360 change your diet and everything, you know. Err but the other thing is that gout
361 definitely has something to do with stress.

362 PC: That's interesting, actually, Robin, because I, I've sort of heard that from other people as
363 well. I don't know if the others think that to be true. Erm ...

364 M: Not in my case.

365 PC: Not in your case.

366 M: Absolutely not in mine.

367 M: I have a fairly stress-free existence.

368 M: Well, lucky you. [laughs] I don't.

369 PC: For you, personally, it doesn't - it's more food related, you would say.

370 M: I, I walk four miles every day and I finish up on a bank, [right] because I go to my
371 daughter, you see, and I think I'd be really crippled with it if I didn't do that. [yes]

372 PC: Right, okay. So ...

373 M: I have to suffer through pain as well, [yes] through doing that. [right] I would have gone
374 today but I've come here instead. [yeah] I have to steel myself and do it. [absolutely,
375 yes]

376 PC: And what's your experience been with the treatment of it, Robin? Because the others
377 have said, you know, whether the anti-inflammatories have done any harm to them,
378 done any good or, you know, what sort of treatment they've had. How about yourself?
379 How have you felt about the initial indometicin and then the allopurinol? Have you had
380 explanations about what they do and so on?

381 M: Yes, yes. But, of course, it was only when the pain became extreme that I started really
382 taking it seriously, if you know what I mean. Erm yeah, I mean yes, I always knew what
383 the drugs did, and I also realised that you mustn't take this indometicin for long or you'll
384 end up with stomach ulcers and worse; kidney stones and you name it. Erm well, as I
385 say, I've more or less got rid of gout now. I haven't any kind of attack - amazingly, I
386 haven't had any attack since I left work ...

387 M: Are you still taking allopurinol?

388 M: Yes, one, one a day because I'm told I've got to take it for life, but if I don't have to I'll
389 stop.

390 M: I mean this - that seems a thing to me, is that like - you wasn't here when I was talking
391 about it, but I took indometicin for 18 months, and ended up with 50% of my kidneys
392 are dead now.

393 M: Really. And you weren't told.

394 M: No. I found out through specialists. They said that had happened and they, they did a
395 lot of tests and they put it down to taking indometicin ...

396 M: Yes, well I was, I was told ...

397 M: Now, I don't knock the doctor for giving it you, but what I'm saying is, to me, is
398 somebody's had it - err several attacks, they should be offered this pill. And allopurinol
399 is a pill with no side effects whatsoever. It's a completely safe pill, they told me, you
400 know.

401 M: And is that the case?

402 M: Oh yeah.

403 M: Is that the case?

404 M: I'm [05:06] ...

405 PC: You're, you're - you find that useful and ...

406 M: I'm absolutely great now, you know, but I think once - if somebody seems prone to
407 producing this uric acid, and they go back to a doctor a couple of times, he should really
408 - you think he'd offer it them, [yeah] being a completely, you know, no side effects pill.
409 [huh-huh] Which he didn't do with me. I had to end up with five weeks in hospital while
410 - which ties in with what you've had, [yeah] I ended up with five weeks in hospital
411 because I stopped taking it, [yeah] you know. It went to my knees, my elbows, and erm
412 since then I've been on allopurinol and the only time that I get flare ups is if I eat
413 something different, you know. That's the only time I get it now. [yeah] Now, when
414 you're talking about erm exercise and that, I mean I, I was playing football until I was 55,
415 [yes] you know ...

416 M: And you changed ...

417 M: I err - well, I, I packed up football ...

418 M: But is that when you got the gout?

419 M: What - it was only sort of - yeah, about five years, four to five years ago, when I was
420 about 57 that I did start getting gout, yeah.

421 M: So you had a change in ...

422 M: I mean I hadn't, I hadn't thought about it in that way, [hmm] because I still do a lot of
423 sport. I play golf three times a week. I swim twice a week, [yes] and that, you know, so -
424 and I've got a manual job.

425 M: Yes, so if you ...

426 PC: Can I just ask people who are not on this long-term treatment err what would sort of
427 make you go on it? Or, you know, when - what is the point, for example Bill said if
428 you're having it currently, you should be offered this tablet. What are your views about
429 that, [06:49]?

430 M: Well, having seen the side effects I don't think I'd want one. Been off tablets anyway, so
431 ...

432 PC: Side effects of what, now?

433 M: What he's on about, kidney disease ...

434 PC: Oh, well that was the anti-inflammatory ...

435 M: That's the anti-inflammatory ...

436 M: Fair enough.

437 PC: So that's not a long-term treatment. The long-term treatment being allopurinol and
438 tablets ...

439 M: I mean allopurinol's supposed to be a long-term treatment. [yeah] What they say is it's
440 got no side effects whatsoever. It's a completely safe pill.

441 M: Right. As I say, I haven't had an attack since May, so [okay] erm if and when I have
442 another one, [yeah] probably when, erm ...

443 M: Can I just say that initially I always had the attacks in my feet. And if it was very bad, it
444 would extend up to your knee. Erm this year in February, when I had gone back to work,
445 because I took the whole of January off, when I went back to work with a stick, teaching,
446 not easy, you know, and I've been doing it for many years, and, to be honest, you know,
447 it was about time for me to finish. Once you've done about 30 years' teaching in
448 schools, you've had your chips, you know. And erm err in mid-February half term err it -
449 I had it still in the feet, can't walk properly, but I'm trying to walk as much as possible,
450 you know, because in fact you have to force yourself to work - to walk. And erm then I
451 started getting it in my fingers and this hand, on holiday in Wales, [08:36]. And so
452 painful you can't sleep. And normally I can sleep like a log, you know. So I'm still going
453 back to work, but here's the vital - to me, it's vital. Erm at this point - what happened is,
454 early February, because of the gout, I fell down some stairs and broke my ribs, right. [oh
455 dear] So I've got the gout in two limbs, one arm and fractured ribs, right. And I'm still

456 going to work because I'm an idiot. And erm - well, to put it in context, at this point in
457 early March - because I know you've got to bear with ribs, you know, [huh-huh] they've
458 got to heal themselves, except you can't sleep at night because you can't turn over. And
459 err at this point, on March the 8th, the headmaster decided, 'We're going to kick this
460 guy while he's down,' and I was subject to the most dreadful bullying by the headmaster
461 of the school. Erm and the following morning I woke up, on March the 9th, and I
462 couldn't move this hand at all. And I had to ring them and say, 'I can't move my hand.'
463 erm, you know, I can't even turn the switch. And they said, 'Well, obviously you can't
464 come to work.' And the previous day I'd been to the hospital to check whether I did
465 have fractured ribs and they'd come with radio [10:15] and they'd come out and said,
466 'Have you ever had an operation on your back?' I thought, 'Oh God, no I haven't.' He
467 said, 'Well, your doctor will get the results within ten days,' and, in fact, I went to see
468 her the following Monday and she said, 'Well, do you want the results, you know? In
469 fact, you've got fractured ribs. You've got gout in all four limbs and you look very tired
470 indeed, Mr Coates, and I think you'd better have a month off.' [hmm] And that was the
471 start of me leaving work, because, in fact, in the end I took four months off and left.
472 [hmm] And that was [10:48]. And I'm still attempting to fight retrospectively the sod of
473 a headmaster, if you'll pardon my French, who brought this about. So the [okay] stress
474 is [yeah] instrumental. I mean I wouldn't have got this inability to move my hand
475 without the mauling that I had from this [hmm] man.

476 M: Going, going back to your, going back to your question, err for me I would medicate
477 depending on the degree of the problem. Erm if, if I had gout to the extent where I had
478 it on my first flare up, where it was extremely painful, if that carried on, then I would
479 want to take longer term medication if it was necessary. And it is. I mean I have these
480 very short duration of flare ups, and not many of them, so I just medicate at that point
481 in time. [right] I think generally I would be disinclined to take any pharmaceuticals long
482 term, [hmm] unless it was absolutely unavoidable. [huh-huh] And if it is unavoidable,
483 you do it because you want to get on with the rest of your life.

484 M: But do you think you'd rather - if, if you kept having these things, that you'd rather be
485 offered a pill that was safe, although it required ...

486 M: Of course you would, yes.

487 M: No, but by using it now. That's what I'm on about. You can keep on having it and if you
488 haven't heard about allopurinol, you just keep on having it, full stop.

489 M: It goes back to medical practice that you're with, and the medical practice I'm with, as I
490 said earlier, are very good at explaining A, what they think it is, B, why they think it is
491 what it is, and C, 'These are the tablets I'm putting you on, and there's no side effects, or
492 it could possibly be these side effects.' The other thing you could do, of course, is when
493 you take pharmaceuticals, there's a little piece of paper printed in 4 point, so you might
494 need a magnifying glass for it, but nowadays [13:03 - participants talking over each
495 other] all prescription drugs list the possible side effects. [yeah] Yeah?

496 PC: Has anyone explained to all of you the rationale behind taking long-term treatment for
497 gout? You mentioned, Bill, to get rid of the uric acid, and are you aware what that might
498 do, apart from stopping the attacks?

499 M: No, no. No, like I say, the only thing I understood is allopurinol prevents your body from
500 making uric acid. [right] It's your body that makes uric acid. [yeah] Some people, if you
501 make a lot of uric acid, that's when you start getting crystallising your joints.

502 PC: Yeah, yeah, absolutely.

503 M: Some people get it to different extents. But from what I, I gathered, allopurinol will stop
504 your body from making uric acid. [yeah] And, to me, that is a far better scenario than
505 taking anti-inflammatories which, which only calm it down [yeah] and stop it
506 temporarily.

507 PC: Yeah. And what's been your erm sort of expectation of the treatment? Or if your
508 treatment - so I want to know what your expectations are, basically, from the treatment,
509 whether whatever you're on has achieved that, and, if not, then, you know, what, what
510 else needs to be done.

511 M: What, the [14:12]?

512 PC: Yeah, or other treatment.

513 M: Well, I mean my doctor says I've got to keep taking these for life, a minimum dose of
514 whatever it is, I don't know. So I take it. [okay] But the really significant thing is one,
515 taking lots of exercise, and the more the better, [huh-huh] literally, diet - well, diet's
516 another thing, but erm lots of exercise and not having stress.

517 PC: So from what you're saying, Robin, drug treatment isn't as perhaps important as the
518 other [14:54 - participants talking over each other]. Is that what ...

519 M: I think it - yeah ...

520 PC: ... other people think to?

521 M: Well, I think it's a combination of the two. I, I think people, when they're getting older,
522 you get overweight, your body isn't as fit, and I think you can alter your diets to suit.
523 I've altered mine. I was diagnosed with diabetes last year, [hmm] last Christmas. I got a
524 very, very high reading. And I altered my diet with that. It's a very low reading now, you
525 know. I only take one tablet but erm it's come down naturally. I think this is possible
526 another thing with gout, is people slightly overweight, for whatever reason, that can
527 possibly make you a bit more prone to [right] producing uric acid. I mean I don't know
528 why, but for whatever reason, it might do. [absolutely, yeah]

529 PC: And then you're - yeah ...

530 M: I've been overweight for - I finished work in the early '90s. I was a relatively fit [15:53].
531 [hmm] I'm now over 20 stone, don't exercise, can't exercise, other conditions. [hmm]
532 Erm I don't particularly cut any food out. I don't know what caused the gout to come.
533 [hmm] I've - nothing I've done different in the last 15, 20 years before the gout came.

534 M: May I say, though, that erm, and I don't know - I'm not making any criticism and I don't
535 know why you don't exercise precisely, but I think you've got to. Erm in January of this
536 year my son is very athletic. He's now 22. We went to Glastonbury, which I really like,
537 and we went to the Tor, you know, and it's a very steep hill. And I was at the bottom
538 and I had, you know, a stick and I couldn't - I could barely put one foot in front of the

539 other. And my son, he ran up to the top. He said - and it's quite a hard run, that. And
540 he said, 'You've got to get up here.' And I walked to the top and I walked down again
541 and I felt about 100 times better, although it was hell.

542 PC: Hmm. So exercise is obviously very important ...

543 M: Oh absolutely critical in my opinion.

544 PC: And how has the treatment of gout had an impact on your life? I mean erm, you know,
545 obviously you've said that the anti-inflammatories had an effect on your kidneys, so it
546 might affect your health other - in other ways. What about other people? Have they
547 had any sort of positive or negative effects of the treatments they receive for it?

548 M: I'm just happy that when I - the last attack I had, the tablets the doctor gave me [hmm]
549 for those five days, it took the pain away. Really did.

550 M: I'm the same, you know. I, I rarely - I don't recall ever taking more than the five tablets,
551 you know. That's [right] the initial hit of two, two the following day and then one the
552 third day. Erm it goes away and I get on with life. So ...

553 M: That's interesting.

554 M: So that's erm fine for me, you know, but I suspect I'm lucky. [okay]

555 M: Well, you're possibly in the early stages of it. That's a possibility.

556 M: Oh yeah, I mean ten years ...

557 M: I mean in three years' time as you're getting a bit older, a bit unfitter, you might start
558 producing more uric acid.

559 M: Well, I'll face that when it comes. [yeah]

560 PC: Ultimately, what do you want your tablets to do for you?

561 M: Cure.

562 M: Take the pain away.

563 PC: Pain away, right.

564 M: There won't be a cure, will there? I think once you start producing [18:38] I think you
565 can - there are certain things you can do ...

566 M: I think if there was a cure, people would already be hooked into it and wouldn't need to
567 research into it any more.

568 M: Well, I'm not so sure about that. I mean talking about, you know, the further effect, erm
569 I'd left work and I think we must be talking about the beginning of October. I left work
570 in mid-July, and instead of going away, I just did almost nothing for about two months.
571 Gradually became more or less normal again. But I was walking in Montgomery. I don't
572 know whether you know but there's a very steep hill behind Montgomery, and I was
573 there with my father's partner and, and another elderly woman, who happened to be a

574 retired doctor, thank goodness. Anyway, we were walking a very steep hill and I
575 suddenly get pains in my chest and I thought, 'Oh God.' Erm fortunately I recognised
576 them because I'd had them previously, but in a milder form. Anyway, so I left them and
577 walking a very steep hill, muddy, and suddenly the pain was like that and I'd got to stop.
578 But I didn't think it was a heart attack. I thought, you know, 'This is odd, you know. I've
579 got to stop and do nothing.' And I did that. Well, the elderly woman, the retired
580 doctor, said, 'It sounds like you've got angina.' So I did nothing for that Saturday
581 afternoon and the Sunday, and I went to the surgery and, after getting a second
582 appointment, they took it very seriously and, you know, heart tests and all the rest of it.
583 And there was nothing wrong with my heart. Err and then I went to the chest clinic at
584 Telford Hospital and erm had a treadmill test err and I seemed to do all right. [huh-huh]
585 And a really excellent bloke, chest doctor, said, 'Well, there's nothing wrong with your
586 heart,' and the surgery had said, 'Well, I think you'd better be careful with this vigorous
587 exercise, you know. You're 64 and a bloke. It doesn't matter if you lose weight and all
588 the rest of it. You, you've a fair chance of having a problem.' They said, you know, 'Just
589 take it easy for a few weeks.' Anyway, the man at the chest hospital says, 'No, no. Of
590 course, you take as much vigorous exercise as you can,' and he said, 'Lose weight.'
591 [hmm] I've known for 15 years that I was overweight. And erm and I, I don't like being
592 overweight. And so I'm really seriously taking exercise and I swim every day and walk
593 and [hmm] cycle and [hmm] I feel very considerably better, I have to say.

594 PC: And what about erm sort of the, the overall impact of gout, not just the treatment, but
595 how has it affected your lives in general? Or the quality of your life, really?

596 M: Go on.

597 M: Not at all.

598 PC: Not at all. Okay, great.

599 M: When I walk - when I have these I [21:52] mobile for how ever long it takes, but when
600 it's gone it's, you know, it's [21:59] just able to have constant pain, so I must admit the
601 pain I get in the hands with gout is absolutely horrendous. Can't touch it. Really hot.
602 [22:13] at all.

603 PC: And how does that affect things like, you know, relationships, work or sort of going out?
604 What ...

605 M: I wouldn't go out if I'd got gout. [hmm] I mean I struggle with mobility now, but, [hmm]
606 you know, gout is err is horrendous. It really is painful. [yeah]

607 PC: Huh-huh. [absolutely] And what about you, Bill? How has it affected your life?

608 M: Well, I still do everything I, I used to do. I've got pain all the time, I have. I have the 200
609 - I have the 100 twice a day, which is 200. And I think if I go back, they'd put me on the
610 300. [huh-huh] And after that, when - where do I go now? [right] If the pain comes
611 back then, what, what is the strength you can go up to? So what I feel in myself, I'll
612 carry on. Although I've got it in my toe now, [right] it wouldn't stop me.

613 PC: So you just get on with it.

614 M: I just get on with it, and I put down in that survey. [hmm] I think ...

615 M: [23:16 - participants talking over each other] tablets interfere with err like the treatment
616 of gout?

617 PC: Well, I was going to come to that. So, yeah, I mean what, what do you think? Do you
618 think other tablets or other medical problems are related with it? Or can interfere with
619 it?

620 M: No. I take five different ...

621 M: I don't ...

622 M: ... tablets a day, you know. [23:34 - participants talking over each other] I wouldn't
623 know if [23:37].

624 PC: Hmm. Has anyone heard anything about that?

625 M: About what?

626 M: About sort of other tablets interfering or bringing on gout or other health problems
627 bringing on gout?

628 M: Other, other medication you take? [yeah] Oh, I don't know. I take medication, but I
629 don't know whether that [23:57 - participants talking over each other]

630 M: You wouldn't really know, would you? [no] An ordinary layman wouldn't really know
631 whether other tablets affect it.

632 PC: Because there seems to be a lot of emphasis, not just from all of you, but other people
633 I've spoken to, about sort of diet and exercise, but, you know, people aren't so
634 convinced about other medical problems or, or sort of tablets that they might be on.
635 And it's interesting that a lot of emphasis is on diet and exercise and, you know, rather
636 than the drug treatment of it.

637 M: I should say that erm, as a result of this erm interlude with the chest pains, they
638 recommended I take amlodipine.

639 M: Amlodipine?

640 M: Yeah. [okay] And this was in early October, I suppose. Well, I resisted. I, I don't like
641 taking tablets of any sort, but I know there are problems with allopurinol [24:55], so I -
642 for two, two months I have not been taking them. It's meant to bring your blood
643 pressure down and ...

644 M: [25:06]

645 M: Yeah. And - do, do you take it as well?

646 M: I've had blood pressure tablets for the last 15 years.

647 M: Yes ...

648 M: [25:14]

649 M: Yeah, well lots of people say, you know, 'Bad luck. You're at that age and it's going to
650 happen.' But erm anyway I went again, only about a week ago, having resisted taking
651 the tablets, because various authorities say erm amlodipine are apparently banned in
652 Holland. There we are. But erm anyway my blood pressure was still high when I went
653 to see the nurse the other week and she - and I said, 'Well, I think I'd better start taking
654 them,' so I'm taking them. I've only been taking them ten days or something. And I
655 don't know, but it doesn't seem to be having any effect at the moment. [okay] It's only
656 minimum dose. [yeah]

657 PC: Okay. Well, what are people's views about - for example, you know, you get screened
658 for cholesterol or blood pressure. [yes] Should you be screened for gout? Should you
659 be [yeah] having a routine test for ...

660 M: I think so. I think so, with gout. Because I mean you can take, you can take blood
661 samples to see if your body is producing it. [hmm] There's no follow up. I mean my
662 doctor will only see me if I go to him. [huh-huh] You know, in 12 months' time - I mean
663 he - the - they send - they probably do with most people now, they'll get in touch me
664 and say, 'You're due for a, a well screening test, your cholesterol and everything,' [hmm]
665 every 12 months. Well I, I had two years with gout and then when I came out of hospital
666 and I went on this pill and it's been great for two years, but the doctor's never contacted
667 me to say, you know, 'Shall we give you, give you a blood test to see whether you are
668 producing anything at all?'

669 PC: So do you not have blood tests at the moment, like on a periodic basis?

670 M: No. [okay]

671 M: What's the, what's the incidence of gout amongst the male population? You said earlier
672 that you couldn't even find any women to take part in the survey. What's the incidence
673 of ...?

674 PC: Well, the overall incidence is about 1.4%, you know, 1.5%, [huh-huh] you know, overall
675 men and women.

676 M: Of the whole population?

677 PC: Of the whole population.

678 M: Really? [yeah] That's quite a lot then, isn't it?

679 PC: Yeah, it, it's commoner than, for example - or, you know, same amount as, for example,
680 rheumatoid, and people don't realise how common it is.

681 M: Hmm. So you're talking about half a million people.

682 PC: Yeah. It, it's, it's very common. And that's why if you look at, you know, the sort of
683 general population that we, you know, in general practices, you get a lot of people with
684 gout and so that's why I was wondering whether you'd sort of come across where there
685 are associations, because it seems to come in sort of grouped with other things, like
686 blood pressure or diabetes, but erm obviously I don't know how much that has been
687 sort of not publicised but how much people know - are aware of that or how much they
688 get told about that, you know. Okay. Erm how do you think we can improve the

689 management of gout in the future? Has anyone had any ideas or thoughts of how you
690 would like it to be done?

691 M: Educate people a bit more about it; doctors educating people about it. [okay] Not just
692 them going to a doctor, they say, 'Oh yeah, you've got gout. Take these anti-
693 inflammatories.' Erm that's [28:30]. So where it's gout, he doesn't explain it, [hmm] you
694 know. When I was in Haywood Hospital they've got it up on the board there exactly
695 what's happening to your joints and [hmm] why, why you're taking this and that. The
696 doctor doesn't. He's just, 'Take them,' and, like you just said, I'll have them and I'm
697 okay.

698 M: Yeah, but that ...

699 M: The problem hasn't necessarily gone away, has it? [hmm] It might come back worse.
700 [yeah] But people say - well like you get a lot of hearsay. Somebody saying, 'Oh, it's rich
701 food.' Somebody saying, 'Oh, it's this.' And that's all that people say. They're not
702 actually as educated in it as they should be, [huh-huh] I, I don't think.

703 PC: Well, what about other people, like, for example, friends or family? What do they think
704 about when you, when you told them you have gout, or if you tell them?

705 M: Oh my, my eldest son just said, 'Ha, ha, ha.'

706 M: Yeah, it's a joke, isn't it? [29:24 - participants talking over each other] A joke.

707 M: You get no sympathy at all.

708 M: You get no sympathy with gout. Good living.

709 PC: Really. You get no sympathy from who? Other people or doctors or everyone or ...

710 M: Oh no, not the doctors, obviously, when you go there. I'm talking if you talk to your
711 friends, [right] your family and all that. [yeah] They all sympathise and then snigger.

712 M: Yes, that's right. Hmm.

713 PC: Why is that?

714 M: I think it's just myth about gout.

715 M: It's like what I said to you, about the old ...

716 PC: And how does that make you all feel then, because you're the ones who have, you're
717 the ones who suffer from it?

718 M: I mean how many people know erm that gout is the third form of arthritis? [right]
719 Unless you're told that it's the third form of arthritis, [yes] and that gout is the most
720 painful form of arthritis, then I'd never have thought that. [yeah] I've got an auntie with
721 osteoarthritis and, and I, I thought that was much more painful. But gout is the most
722 painful form of arthritis you can have. People aren't aware of that.

723 M: Is it age dependent? I mean we're of an age round this table. [huh-huh] Why aren't
724 there 20 year olds sitting here?

725 PC: Err it is commoner as you, as you grow older. But it is seen in younger people as well,
726 but they are sort of special cases where they might have a metabolic problem ...

727 M: But it predominantly is - it's predominantly with more mature persons.

728 PC: Yes, yeah.

729 M: But you can't say yes.

730 M: It might be a daft question, but is there anything to say it could be hereditary or
731 anything like that?

732 PC: Well, we, we'll come to that after the end of the interview, but what does - what do
733 other people think about that?

734 M: I've never known any hereditary ...

735 M: Actually, that's not quite true because I'm forgetting something. In fact, my mother died
736 relatively young, at the age of 57 and she dropped dead of a stroke. Erm and, in fact, in
737 the last two years of her life she did have what was diagnosed as arthritis, but I think it
738 could well have been gout, as a matter of fact. But we're talking about quite a long time
739 ago and it could have been [hmm] gout. [hmm] So it - but in her case I think it was also
740 environmentally induced rather than - there's a long story behind that.

741 M: My father, he, he - mine's hereditary. [okay] I mean it certainly wasn't drink, because
742 he didn't drink, so [yes] that one's in my case.

743 M: Yes, that's right, yeah.

744 M: Yeah, there's no history of gout in my family at all. [okay] Absolutely not.

745 PC: Okay. And why - do you have any thoughts on why people don't like taking treatment
746 for it? Why do - because we know that the treatment, especially the long-term
747 treatment, uptake is very low. What do you think puts people off that?

748 M: [32:16 - participants talking over each other] We don't know what damage you're doing
749 to yourself, do we, really. [okay]

750 M: Yeah, that may be ...

751 M: It's like painkillers, isn't it? I, I never - all the way through it, I never took painkillers.
752 [okay] I mean I should [32:30] but I only think, you know, if you've got to take them
753 you've got to take them, but I only think it just masks it, [yeah] you know, and you don't
754 want to mask things. [yeah] If it's there, it's there.

755 M: I should go back, you see, to the surgery and tell them, but obviously it's going to put me
756 on high dosage, and what is it going to do? And the thing is, what is the highest dosage
757 you can have? And then what, what happens after that?

758 PC: Right, so you have all these uncertainties in your mind.

759 M: Yes, all those uncertainties. There's another thing I read in the Mail on Tuesday, the
760 medical part, where people won't take this for cholesterol, these pills for cholesterol.

761 They're all packing them in because have they got gout, or is it caused through this
762 treatment for cholesterol?

763 M: Statins.

764 M: Pardon? Yeah, statins. They're all going back and saying they're getting pains through
765 statins and they're dropping them off. So I goes along and says to this nurse, and she
766 says, 'Well, just have them every other day.'

767 M: The newspapers are full of contradictory advice. I mean [yeah] I like drinking red wine
768 and I always feel like clipping out - because every three months there's a little report in
769 there that says, you know, 'A glass of red wine every day is good for you.' Two months
770 later, 'Red wine, if you drink a glass a day, it will kill you in 40 years.' You know, given
771 that I'm 64 ...

772 M: You'll take a chance.

773 M: ...I, I'll take a chance it will kill me in 40 years. So there's, there's all the contradictory
774 comments out there. [right] I think it comes back to you as an individual much more
775 and what your view, what your personal feelings are. [yes] I'm reluctant to take
776 pharmaceuticals long term, unless it's absolutely necessary. And yet I'm sure if I
777 developed in 15 years' time very severe gout and the doctor said, 'Well, take one of
778 these every day for the rest of your life and it will cure the problem.' And if the
779 pharmaceutical gave me back my life, in other words it didn't inhibit my life in any way,
780 I'd be quite happy to take it every day. [hmm] Yeah.

781 PC: Do people feel it inhibits their life, taking medication for gout?

782 M: Pardon?

783 PC: Do people feel it inhibits their life in any way, taking the medication for gout?

784 M: Not at all.

785 PC: Because Ian's just said that, you know, if it didn't inhibit their life, then he might take it.
786 So ...

787 M: So - I mean going back a little bit, I mean err when you were saying about your doctors
788 not informing you of possible side effects, I, I should say that the doctors I've met have
789 all been extremely good. [huh-huh] But erm I don't know. I don't know if a lot of it's to
790 do with getting older, to be honest. I mean [okay] all kinds of things are beginning to go
791 wrong, as it were, you know.

792 PC: If someone told you ...

793 M: These things happen, you know.

794 PC: Right, so you just accept it.

795 M: Well, there's - and going back to the alcohol thing, I mean I like a drink, but, you know,
796 you've got to be careful. I actually gave up drinking wine, because it's so delicious,
797 about - more than a year ago and I - over a long period I, I cut it down and I don't drink
798 wine any more at all.

799 M: [36:01] about keeping the average up. [laughter]

800 PC: Why is that, Robin? Why don't you drink it any more?

801 M: Oh, all kinds of reasons.

802 PC: Okay. So not related to the gout.

803 M: Oh, partly related to the gout, [right] yes. Yes. [right] I mean - and, in fact, one of my
804 doctors, Doctor [36:18], said, 'Distinguish between different types of alcohol,' and said,
805 'Well, you ...' Erm I said, 'I like beer, you know. I'm not going to stop drinking it.' And, in
806 fact, another bloke has said, 'Cider's good for it.' [laughs] Because he's got gout and he
807 drinks as much cider as he can get down. [right] He, he's quite happy with it.

808 M: It's all confused. [36:43 - participants talking over each other]

809 M: But I mean the beer, the doctor said, 'Well, you can drink mild but you can't drink bitter,'
810 and, you know, that kind of thing.

811 PC: Right, right. So - and what if erm you were told that taking long-term treatment for gout
812 would prevent irreversible bone damage or it would prevent, you know, heart disease,
813 that sort of thing. Would that change your mind? Would that make you sort of more
814 amenable to taking it maybe? I don't know.

815 M: If it didn't have any side effects, I'd like that.

816 PC: So if it didn't have side effects, plus it had all those advantages, you, you would consider
817 it.

818 M: Hmm. If it could be guaranteed no side effects, then yeah. There must be [37:28] side
819 effects.

820 PC: Yeah, it is, yeah.

821 M: If somebody promised me eternal youth I'd be extremely suspicious.

822 PC: Right, okay. [absolutely] Okay. Okay. Erm fine, so any, anything else that any of you
823 want to add about the treatment or your diagnosis or, or sort of how it's affected your
824 life in general?

825 M: I think you can see from here that everybody's got a different idea [yeah] and
826 everybody's got different things that - it's all hearsay. People are always looking for
827 hard and fast answers, aren't they? Don't do this. Don't do that. [hmm] If you don't do
828 that, you'll be all right. [hmm] But with gout, there's a lot of things that contribute to it.
829 You, you've mentioned exercise and things like that. Well, that's the same with most
830 things in, in life, isn't it, you know. If you're not looking after your body, then it can
831 affect you producing acid and it can affect you doing other things. But the food part of
832 it, a lot of it is a - well, some of it, like I found out, isn't hearsay. I mean the other week -
833 I never had it in my hand before ...

834 M: Do you know what I ...

835 M: ... these fingers went twice the size [yes] of my knuckle and I couldn't do anything. [huh-
836 huh] And I'm thinking, 'Is it gout? Isn't it?' And I ...

837 PC: So what did you do to ...

838 M: I took my colchicine tablets [right] and two days later it had gone. [right] So I presume
839 it's gout. And then I thought back to four days, up to four days before I had it, and I had
840 one thing different; I'd had a Chinese. [right] And somebody I know says to me that
841 they use a calcium something, bit weird, I don't know what it is, that can affect things
842 like arthritis and [okay] stuff like that. So I always find that there's something I've had
843 that's caused it, [yeah] [right] you know, something out of the ordinary. Apart from
844 that, I don't have any problems whatsoever now.

845 M: One of the things I'm surprised that hasn't come up is this idea that if you, you drink
846 enough water it, in effect, pushes you through. Because you're going to the loo a lot
847 more, you, you don't - your uric acid level drops. Now, I don't know whether that's
848 myth or reality. Erm my, my wife's fairly pragmatic, but she drinks a lot of water and she
849 said she thinks the answer to my occasional flare ups is I should be drinking at least four
850 or five pints of water a day. [right]

851 M: And do you agree with that?

852 M: Erm if, if there was evidence, I might drink more water, without the red stuff in it.
853 [laughter] [yes] Is there any evidence that raising the level of your water intake lowers
854 your uric acid?

855 PC: Well, there, there are theories about how dehydration may bring it on, but there's - I
856 don't think there's any conclusive evidence about that. [right] So yeah. And what
857 would you say if you met someone who'd just been diagnosed with gout? What advice
858 would you give them? What would you say to them?

859 M: Oh, I - I mean well, it depends what symptoms they were having, you know. People are
860 ...

861 M: I'd give them that. [right] I'd say, 'Get yourself some of those and [40:47].'

862 M: I'd say, 'You get fit and erm, [yeah] you know, get fit and stay fit.'

863 PC: And you would say, 'And take those naproxen tablets.' Bill, any word of advice from
864 you?

865 M: I don't know. Listen to the experts, I would say. [okay]

866 M: I would say, I would say it should be up to the doctors, shouldn't it?

867 PC: Should be up to the doctors ...

868 M: Doctors should make people more aware [okay] of what sort of things that can help,
869 [okay] you know. Not just uric acid [41:18] done, you know. He could turn around and
870 say, 'What about your eating habits? Do you think you could alter them a bit? Can you
871 eat healthier?' [huh-huh] But, you know, they're the sort of things doctors could say to
872 people, that it might help. A lot of people will try it to see if it does help, you know.

873 PC: Okay. Right. And I just want to pick up on a couple of points that Bill and erm Ian have
874 raised, that you stop the allopurinol when you feel an acute attack coming on, [yeah]
875 and you [yeah] took 500 times two on the first day of that ...

876 M: Well, only taking the colchicine tablets.

877 PC: Who told you about - who told you to do these things?

878 M: I, I was told from day one from the hospital when I took [right] allopurinol that if I got a
879 flare up, that I must take the colchicine tablets ...

880 PC: And stop the allo ...

881 M: I must stop the allopurinol ...

882 PC: And when do you go back ...

883 M: ... because that can aggravate it now, when you're in an attack. And I - what I do, I
884 spend about two, two to three days, [okay] usually it's gone within the three days.
885 [okay] And then after that start taking it again.

886 PC: And when you start taking allopurinol again, do you take the colchicine with it?

887 M: No.

888 PC: No. You just start the allopurinol on its own.

889 M: The only thing they said was, was erm don't just stop the colchicine straightaway. [huh-
890 huh] If at the end of the day it feels as if it's gone, don't stop it straightaway. Always
891 take two to three days ...

892 PC: But you never take the two together.

893 M: No.

894 PC: Right. And ...

895 M: This idea of taking the two pills initially, then moving on to prescribed dosage, was
896 suggested by the doctor. [right] Take two as soon as you get them and two a day. And,
897 as I say, by day three I took the suggestion because it's - it's 95% gone, but I will just take
898 the extra one to ...

899 M: Do, do you still get acute attacks? Oh, you don't.

900 M: I was saying before you arrived, I've probably had gout three or four years and I've had
901 what I consider to be two severe attacks. But for me, a severe attack is over and done
902 with and gone within three days.

903 M: I see. But you've only the two attacks ...

904 M: In, in three or four years.

905 M: And you don't have a general sort of low-level ...

906 M: No.

907 M: No, I see.

908 PC: Do your family members get sort of - what, what's their feeling when you have an acute
909 attack of gout? What - does it affect your relationships?

910 M: Yeah, get on with your life. [yeah]

911 M: It's the only time I get sympathy, when I've got gout. [right]

912 M: Well, I live on my own so erm so I have to deal with. [okay]

913 M: My wife's very supportive. [okay] Only because she knows how painful it is.

914 PC: Right. But other people outside that closed knit circle, you said laugh when you, when
915 you ...

916 M: They think it's a joke, [yeah] because gout is a rich man's disease.

917 M: Actually people who've had any experience of gout said, 'Oh God, that's incredibly
918 painful.' It isn't everybody who's unsympathetic. Some people are very ...

919 M: Oh yes.

920 M: ... sympathetic.

921 M: I had a chap who brought me some pills down, [yeah] with crutches.

922 M: You can say that about lots of diseases. Touch wood, up until 1992 I suffered very badly
923 with back pain, and that never drew any sympathy because, you know, back pain can be
924 everything from swinging the lead up to completely crippling. [yeah] And so you got a
925 very mixed reaction off people about back pain. And I think gout's a bit like back pain.
926 Another thing people laugh at his haemorrhoids. [huh-huh] So I don't think it's just gout
927 that gets a very mixed reaction. Back pain and haemorrhoids are the same. [absolutely,
928 yes]

929 PC: Does it stop people from reporting it for, you know, if people are err laughing at it,
930 would you think it would stop people from telling their doctor that, 'Look, this is what
931 I'm getting'? Are people ashamed of bringing it up?

932 M: I think gout is so severe, it hits you. You wouldn't care if everybody in the land was like
933 that. [45:27 - participants talking over each other]

934 M: Actually you are remarkably immobilised. A whole day sitting in a chair doing nothing.

935 PC: Right, okay.

936 M: Some people find it hard to believe, like when I get it, there's a - within a day, within two
937 days, I can't walk without a stick. [hmm] I mean I, I walk with a stick because I can walk
938 then, but without a stick I can't, I can't walk at all. [right] Can't cross the floor. It
939 happens so quick, people just don't believe it. [yeah]

940 M: That's the reality of gout. I remember when I had it for - I was in bed for three days and
941 I when I went to the toilet I put the brush under me [46:07] [yeah] to get in the toilet.
942 [right]

943 M: I also found when, when you lie in bed, even the pressure of the [46:13 - participants
944 talking over each other] sheets give you pain. [yeah]

945 PC: And there were some interesting thoughts from you that erm it was like haemorrhoids
946 or like back pain. Any, any other condition that you sort of can compare with gout or -
947 what I'm trying to assess is, do you think gout's given the importance that it should be?
948 Or, you know, how do you feel about that?

949 M: I don't know in a general sense. However, I mean I go to a pub regularly called [46:46]
950 and a lot of the men of, let us say, over 45, quite a lot of them have got gout. [hmm]
951 And erm, you know ...

952 M: I think, I think it's - I - from the stories round the table I appear to be very lucky, you
953 know. Two attacks, four years, go very quickly. I'm sure at the other end of the
954 spectrum there are people who are severely disabled [yes] [hmm] and so I, I don't think
955 there's one answer, because I think if you're at the severely disabled end of the
956 spectrum, erm then I, I - the questionnaire I did, erm some of the questions seemed to
957 be lifted straight out of the application form for disability allowance, erm which I have
958 some experience of. [okay] Erm and I'm sure there are some people who are so badly
959 afflicted that their, their life erm, you know, they've got to give up work and all the rest
960 of it; they are genuine disabled. But I think that's true of all illnesses. You know, there's
961 a spectrum from the very [yeah] 'Oh twice in two - twice in four years, you don't know
962 what you're talking about,' through to totally disabled. So I don't think gout is any
963 different from any other disease in, in that respect. If you've got it very badly, you
964 know, it's life debilitating. [yeah]

965 PC: Do you feel people see you as, as such, in - because two attacks in four years, you don't
966 know what you're talking about. If you meet people with severe gout, is that how they
967 perceive you?

968 M: I've never [48:22]. These guys are the only people I've met [okay] who have got
969 significant problems with gout. [right, okay] I've never met anybody who's, who's right
970 down the disabled end of the spectrum. [okay] But I'm sure somewhere there must be
971 people who are, you know, who can't walk, you know. They can't work, they can't walk,
972 [hmm] they can't get out of the house. They're totally dependent on other people to
973 cook for them [hmm] and shop for them. Erm there must be people like that. I've just
974 never come across them.

975 PC: Okay. And it's interesting that all of you mentioned about articles in the newspaper
976 about gout. Do you - because that's sort of, you know, not in perhaps a very positive
977 way. It might be a cartoon. It might be conflicting advice or whatever. On the other
978 side, do you think they could publicise it so that people are educated? You know, what
979 you were saying, Bill. For example you see campaigns on TV about, you know, heart
980 attack or cancer or whatever. Do you think it should be a similar sort of thing, because
981 it's common and, and severe in some people?

982 M: Is it that common when you take it up to the level of heart attacks and cancer and ...

983 PC: Erm ...

984 M: Is it, you know, heart attacks, cancer up here and gout down here and ...

985 PC: Well, it depends how you, how you look at it, because you could look at it in terms of
986 numbers, or you could look at it in terms of severity and pain and association with other
987 things. So I suppose you could have ...

988 M: Well, I've had sciatica and err it's similar. Sciatica's terrible [yeah] as well. [okay]

989 M: I don't, I don't - I should imagine that gout is not very sexy when it comes to getting
990 grants or money for research, you know. If you, if you want big money for medical
991 research it's got to be cancer or heart or, or something like that.

992 PC: That's really interesting. Why do you say that?

993 M: Well, because it - I don't think it's perceived to be life threatening, whereas cancer and
994 heart attacks are. [right] Erm I'm aware of cancer charities and heart charities. I don't
995 ever recall coming across a gout charity. I, I've seen arthritis charities, but not gout
996 charities. [that's right] And so I - and it's, you know - out there in society, erm it's -
997 there are hierarchies erm and I don't think it appears on the hierarchy [no] in the same
998 way that we have a Royal Society for the Prevention of Cruelty to Animals, [yeah] but
999 there aren't royal societies that I'm aware of for people's diseases. You know, I mean it
1000 's just the way [hmm] the society is in this country. You tell me, is gout sexy when it
1001 comes to research grants, you know? Can you - does money flood in to your research
1002 grant or do you have to fight tooth and nail for it?

1003 PC: Yeah, it's - I think you're, you're right and, you know, I think we're getting [51:27] but I
1004 can see other centres and other departments who struggle with it. Erm and, you know, I
1005 - it's interesting about what you said about the charities that are set up for different
1006 things, and I'm not sure if any of you are aware, but the arthritis charity - for example,
1007 Arthritis Research UK, which provides a huge amount of funding, that also supports
1008 people with gout. So perhaps it's kind of buried in a spectrum of other arthritis, rather
1009 than an individual thing on its own. Erm ...

1010 M: See, I didn't even know it was a form of arthritis. [yeah] I just thought it was crystals in
1011 your joints.

1012 PC: Yeah. Yeah, that's true, but not many people do know that. Okay. Any final thoughts
1013 from any of you about anything else that you want to bring in, your own experience or
1014 otherwise, really?

1015 M: I, I've got a question. What are, what are you hoping to achieve is the - or what is the
1016 planned outcome of the research that you're doing?

1017 PC: Okay. I'll erm tell you that in a second, if that's okay, and I'm just going to switch these
1018 off before we talk about that specific bit.

1019 M: Is there - is that the end of it now? Or is there some sort of follow up?

1020 PC: You mean for the study?

1021 M: For us.

1022 PC: Err there is follow up.

1023 M: For us?

1024 PC: Yeah, for you. So if we've stopped talking about sort of the gout, the treatment and
1025 impact of gout, then I'll just switch these off and we'll - is that okay with everyone?
1026 Anything else you want to add?

1027 M: Yeah, no. It will be okay.

1028 PC: No? Okay. Right, let's just ...

1029 End

Appendix 13: Application for peer review of research protocol

Keele University
APPLICATION FORM FOR INDEPENDENT PEER REVIEW

Instructions

The application form should be completed as concisely as possible and should address the points as applicable. Please state clearly if any section is not applicable to your project. Most of the sections are the same as the Integrated Research Application System (IRAS) form. The boxes can be expanded and text can be 'cut & pasted' to/from the IRAS form. For convenience we have indicated the relevant IRAS question numbers that map to this form.

Once your application form has been completed and signed off as appropriate, please forward an electronic copy and hard copy to Nicola Leighton, Research Governance Officer, Research & Enterprise Services, Dorothy Hodgkin Building, Keele University, ST5 5BG, e-mail n.leighton@keele.ac.uk.

If you have concerns regarding the disclosure of original research and the risk of plagiarism during the review process please contact the Chair of the Independent Peer Review Committee via Nicola Leighton 01782 733306.

Please note that the Independent Peer Review Committee is not linked nor is a sub-committee of a NHS Research Ethics Committee (REC).

Administrative Details

Full title of the research project: Prospective observational cohort study of health related quality of life and chronic foot problems and their determinants in gout

Short title of the research project: The health related quality of life in gout study

Key words: Health related quality of life (HRQoL), gout, foot problems, health status indicators, outcome assessment, patient reported outcomes, cohort, observational study, patient experience, epidemiology, qualitative research, mixed-methods.

Name of Principal Investigator: Dr Priyanka Chandratre

Current Post: Clinical Research Training Fellow / Honorary SpR in Rheumatology

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Name of Chief Investigator: Dr Edward Roddy

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Other Members of the Study Team (if there are more than 3 members please keep adding to this section)

Name: Prof Christian Mallen

Post: Professor of General Practice

Arthritis Research UK Clinician Scientist

Organisation: Arthritis Research UK Primary Care Centre

Role in Study: Research co-supervisor and GP expertise

Name: Dr Jane Richardson

Post: Senior Lecturer in Health Services Research

Postgraduate Research Director, Institute for Primary Care & Health Sciences

Organisation: Arthritis Research UK Primary Care Centre

Role in Study: Research co-supervisor and qualitative methods expertise

Name: Dr Sara Muller

Post: Research Associate in Clinical Epidemiology

Organisation: Arthritis Research UK Primary Care Centre

Role in Study: Statistical advisor

Name: Prof Keith Rome

Post: Professor of Podiatry

Organisation: AUT University, Auckland, New Zealand

Role in Study: International collaborator and Podiatry advisor

What is the principal research question /objective? *Provide a clear account of the purpose of your investigation, including primary and secondary objectives (A11 of IRAS form)*

The main objectives of the study are:

1. To estimate the prevalence of poor HRQoL in patients with gout and its distribution by demographic, socio-economic and anthropometric characteristics (cohort study – baseline data).
2. Describe the prevalence, onset, persistence and progression of chronic foot problems in gout over 3 years (cohort study – baseline and follow-up data).
3. To examine:
 - a) Cross-sectional associations between poor HRQoL and frequency of gout attacks, chronic foot problems, co-morbidities, gout treatment, and psychosocial factors in gout (cohort study – baseline data).
 - b) Change in HRQoL in gout over 3 years and determine which of the associated factors may predict deterioration (cohort study – baseline and follow-up data).
4. To explore patient experience of gout focusing on impact of gout and its treatment on HRQoL (cohort study – nested focus group interviews).

Scientific background What is the scientific justification for the research? *What is the background? Why is this an area of importance? Has similar research on this topic been done before? Have all existing sources of evidence, especially systematic reviews been fully considered? What new information will it provide? (A13 of IRAS form)*

Gout is the most prevalent inflammatory arthropathy, affecting around 1.4% of the adult population in the UK (1). It is caused by monosodium urate (MSU) crystal deposition in and around joints once the physiological saturation threshold in body tissues for uric acid

is exceeded. The most commonly affected joints are the 1st metatarsophalangeal joint (MTPJ), mid foot and ankle. The first acute attack affects the first MTPJ in 56-78% of the patients with 90% having acute gout of the great toe at some point in their disease course (2). Gout also associates with hallux valgus deformity as well as chronic pain in the great toe (2). One further small hospital-based study has shown more frequent gait impairment and foot-related functional problems in gout than controls (3). With the exception of these two studies, there is little evidence from primary care about the potential long term consequences of gout as far as foot problems are concerned. Gout is an important condition not only because it is an excruciatingly painful acute arthropathy but also because of its associations with chronic disease states such as metabolic syndrome, osteoarthritis and renal and cardio-vascular morbidity (4).

In the face of such significant associated disorders, it is often difficult to attribute disability or diminished lifestyle to gout. This may be an explanation for the relatively sparse literature available around health related quality of life (HRQoL) and disability in gout patients (5). Most studies to date have had limitations such as small samples, cross sectional design and the use of generic instruments (which predate the disease specific Gout Impact Scale (GIS)) to measure HRQoL (6). Little is known about the changes in HRQoL in gout patients due to the lack of longitudinal follow up. However, severe chronic gout, through its frequency and severity of episodes and recurrent pain, may have a great impact on patients HRQoL. These symptoms, which may affect the patient's emotional, social and physical functioning, result in significant disability. Factors directly related to gout symptoms, as well as those related to disease complications and adverse effects of gout treatment, all potentially contribute to impaired HRQoL. Cross-sectional epidemiological studies in primary care have also shown that gout has an independent association with impaired HRQoL, particularly affecting the physical domain, after adjustments for co-morbidities such as osteoarthritis and vascular disease (7, 8). This finding is not unique - there are other studies emphasising the significant effect of 'treatment failure' gout within a hospital-based gout cohort on patient HRQoL and disability, especially in the realm of physical functioning (5). In a 52 week prospective observational study, although co-morbidities contributed to impaired HRQoL, the scores were substantially lower than for the normative US adult male population, even for subjects who did not have any other illness (5). The same multi-centre prospective study demonstrated that the patients' perception of disease severity correlated more closely with HRQoL than the physicians' assessment of disease severity. Patients and healthcare providers often have different priorities as far as the optimal management of gout is concerned (9). A cross sectional qualitative study assessing the views of patients and physicians highlighted marked differences in what is important to each group. Whilst the physicians regarded pharmacological treatment of gout to be effective, most patients discontinued treatment due to adverse or no positive effects, paradoxical flares and financial constraints. Patients also expressed lack of understanding of gout, a disease

physicians felt was easy to comprehend for the patients. Health care providers felt they had adequate training to educate patients about disease self management, an area patients wanted to know more about. A recent qualitative study (10) on the impact of gout highlighted the lack of understanding and the stigma associated with this condition which often leads to under reporting of symptoms. This in turn can lead to suboptimal treatment despite disease severity.

These findings are not surprising given that, until recently, there has not been much published work on the implications of gout in terms of morbidity and mortality as well as associated healthcare utilisation and costs (11). The majority of gout is dealt with within the primary care setting, yet most of the research to date has taken place in secondary care which may deal with more complex and atypical presentations including those who have failed to respond to or not tolerated standard therapies. Therefore the applicability of such data is questionable in the wider setting of the community. There are several issues around the management of gout which need better understanding through robust research. At present it is estimated that only 30% of patients take definitive treatment (e.g. allopurinol) for gout in primary care (12, 13). This is despite recommendations from international guideline groups which advocate the use of urate-lowering therapies (ULTs) such as allopurinol to lower uric acid levels, shrink tophi and prevent acute attacks of gout (14, 15). There is no clear explanation for the discrepancy between the recommended and actual treatment of gout, although the potential for drug toxicity, interactions and polypharmacy associated with co-morbidity might reduce uptake of long-term treatment. International treatment recommendations suggest that patients experiencing two or more attacks in a 12-month period should be offered ULT but this recommendation is based upon expert consensus rather than empirical research evidence (15, 16). Improving understanding of which factors predict outcome would help substantiate indications for ULT and identification of patients at which this should be targeted. Hence there is a need for a well-designed and conducted prospective observational cohort study in primary care which incorporates patient reported outcomes (PRO) to assess long term outcome and consequences of gout, focusing particularly on HRQoL and foot problems.

Study Type (please highlight in bold as many as are appropriate)

Randomised controlled trial	Yes / No
Controlled trial without randomisation	Yes / No
Pilot	Yes / No*
Please see definition of pilot study at end of form	
Case control study	Yes / No
Cross-sectional study	Yes / No

Quasi-experimental	Yes / No
Before and after study	Yes / No
Survey	Yes / No
Cross-over study	Yes / No
Qualitative	Yes / No
Cohort	Yes / No
Observational	Yes / No
Other	Yes / No
If other please give details	

Is the research being undertaken as part of an educational course or research degree?
Yes / No

If yes, please provide the following details:

This proposal seeks peer review for a 3 year prospective study in which a PhD will be nested using baseline data only.

Name and level of course/degree: PhD in Primary Care Sciences

Name of educational establishment: Arthritis Research UK Primary Care Centre, Keele University

Name of supervisor: Dr E Roddy, Prof C Mallen, Dr J Richardson

Plan of Investigation

Summary of study *Give a brief synopsis/summary of methods and overview of the planned research. A flow chart or diagram should be attached where appropriate. It should be clear exactly what will happen to the research participant, how many times and in what order (A14 of IRAS form)*

This is an observational epidemiological study using self-completion health survey questionnaires over a period of 3 years.

The study has the following data collection time-points:

- Phase 1: Baseline postal questionnaire
- Phase 2: Review of general practice medical records
- Phase 3: Focus group interviews (nested purposive sample)
- Phase 4: Follow-up mailed survey at 6 months
- Phase 5: Follow-up mailed survey at 12 months
- Phase 6: Follow-up mailed survey at 24 months

- Phase 7: Follow-up mailed survey at 36 months

The design of the study is summarised in a flow chart in appendix 2.

Study population (A16 of IRAS form)

All adults (aged >18 years) registered with 30 general practices in the West Midlands who have had:

- A consultation for gout in the preceding two years or,
- Prescription for colchicine or allopurinol in the preceding two years.

Inclusion criteria *What inclusion criteria will be used to select participants/patient records/tissue or bodily samples (list cases and controls separately if appropriate)? (A17 of IRAS form)*

- Registered with the participating general practice during the study
- Read code consultation for gout or prescription for colchicine or allopurinol during the preceding two years
- Provided written informed consent for participation in the study

Exclusion criteria *If you are excluding participants on the basis of age, sex or ethnicity please explain why (A18 of IRAS Form)*

- Under 18 years of age
- Vulnerable groups – e.g. significant cognitive impairment, severe enduring mental illness, active malignancy or other terminal illness.

Will the study involve the recruitment of human research participants? Yes / No

Study Setting *(name and description of centres)*

The study participants will be recruited from 30 general practices in the West Midlands. Qualitative focus group interviews will be held at the Arthritis Research UK Primary Care Centre (ARUKPCC).

How will potential research participants in the study be identified, approached and recruited? *(Give details for cases and controls separately if appropriate, describe sampling methodology and randomisation procedures) (A28-1, A28-2, A29, A30, A32 of IRAS form)*

Patient identification

All potentially eligible patients registered within the participating general practices will be identified through standard Read codes used for gout or prescription of colchicine or allopurinol. The following Read codes are used by the ARUKPCC:

Code	Term
C34	Gout
N023	Gouty arthritis
EGTON 227	Gout NOS
OX2740G	Gout Acute /ox
1443	H/O: gout
EMISR4QG01	Gouty tophi + Gout NOS
2D52	O/E - auricle of ear - tophi
669	Gout monitoring

Staff from the Keele Primary Care Research Network will conduct a one off electronic search of the primary care records in participating practices to identify patients with a consultation for gout or a prescription for colchicine or allopurinol within the last two years. The names and contact details of the eligible patients will be stored in a password protected mailing database and held on the university's firewall and password protected server. No other information from the patients' primary care records will be accessed or stored unless and until informed written consent to do so is obtained from the patient. The Primary Care Research Network team members will screen the mailing lists (prior to mailing) for patient deaths and departures from the practice to ensure that patients are not inappropriately contacted. The lead general practitioner (GP) at each practice will be invited to identify potentially vulnerable patients to be excluded.

Initiating patient contact

All eligible patients will be sent a study pack from their general practitioner (on general practice headed notepaper). This will contain a letter of invitation, participant information sheet (PIS), a pre-paid return envelope and a baseline self-administered questionnaire which will also include a consent form asking for consent:

- a) For further contact by post
- b) For review of their medical records

Potential participants will also be provided with a contact name and telephone number should they have any queries about the study. Patients will be informed that they are under no obligation to participate and that if they decline their normal clinical care will not be affected in any way. On return of the questionnaire the response is recorded against a unique patient number – this will include completed questionnaires, contact details, request to be excluded from the study and non responders. Participants returning their questionnaires with the consent sheet and those who wish to be excluded

from the study (non-consenting responders) will be logged on the database so that no further reminders are sent to them. The mailing database will determine future mailings. By including the consent form with the questionnaire we are hoping to avoid the wasteful exclusion of completed questionnaires but incomplete consent forms thereby preventing any adverse effects on data quality.

Non-responders to mailed study pack

As per the ARUKPCC questionnaire mailing Standard Operating Procedure, non-responders are sent a reminder postcard at two weeks and a reminder letter with repeat baseline questionnaire two weeks later (4 weeks after the first questionnaire) (17). This approach maximises response without placing significant burden on patients. Those who fail to respond after all three baseline mailings will be assumed not to have consented to the study and will not be contacted again.

Will informed consent be obtained from the research participants? Yes / No

(Give details of who will obtain consent, how it will be done, and of any particular steps other than an information sheet taken to provide information e.g. video, interactive media. Please attach a copy of the consent form. If consent is not to be obtained, please explain why not) (A31-1 of IRAS form)

Following identification through standard Read codes, patients will be contacted by post. The information pack will be sent from the general practice, and will contain a cover letter, PIS and a questionnaire with the consent form at the back. This consent form will ask permission to be contacted again by post and for medical record review. Those wishing to participate in the study after reading the information provided will be asked to return their completed questionnaire and signed consent form back to the ARUKPCC. Should a questionnaire be returned without the consent form, the medical records of the patient will not be accessed and they will not be contacted again.

Subject/patient participation

(Provide details of what research participants will do e.g. treatment intervention, completion of a questionnaire, participate in an in-depth interview; provide details of how the research procedures or intervention will be administered (include duration and audit details); provide details of any risks to the participant and safeguards to be put in place) (A19, A20, A21, A22, A23, A24, A26 of IRAS form)

Phase 1: Baseline postal self-administered health survey questionnaire

The questionnaire will be divided into 7 main sections:

- a) About gout symptoms and treatment
- b) The impact of gout on daily life

- c) General health (including co-morbidities and measures of physical function)
- d) Measures of anxiety and depression in gout patients
- e) Foot and other joint problems
- f) Occupational characteristics
- g) Socio-economic and demographic characteristics

Details of the conceptual domains, operational definitions and empirical measures are provided in appendix 1. The completed baseline questionnaires will have the responses securely stored in the study database. This database will be used in cross-sectional analyses where appropriate.

Phase 2: Review of general practice medical records

All participants in Phase 1 who give permission for their GP records to be accessed will have their computerised medical records tagged by a member of the Primary Care Research Network. All consultations for the 24-months prior to study entry and then prospectively for the three-year study period will be identified. The practices participating in this study are fully computerised and undergo annual audits completed by the Primary Care Research Network to assess the quality and completeness of the data entry at the practices (18). All relevant gout related consultations or prescription for colchicine or allopurinol will be identified using search techniques based on Read codes and free text entries. Such searches have already been developed and successfully applied for foot and knee-related consultations in the Centre's cohorts (19-21). Full medical records of the consenting participants will be accessed for information regarding co-morbidities, other musculoskeletal problems, repeat consultations in primary care for gout (clinician recorded diagnosis mapped to standard Read code morbidity codes), prescription patterns and referral to secondary care. All sensitive data (name, contact details) will be removed from the medical records and the consultation data will be linked to the survey and clinical assessment data by unique survey identifier.

Phase 3: Focus group interviews

A sub sample of approximately 20 patients from phase 1 will be identified using purposive sampling (for example, pattern of joint involvement, demographics and scores of HRQoL instruments in the baseline questionnaire) and invited for a qualitative focus group interview with a researcher trained in qualitative research methods. The researcher from a clinical background will have received special training in qualitative research methods with a particular emphasis on focus group interviews. The focus of the interview will be to discuss in greater detail the themes arising from the self-completed questionnaires. The objective of the interview will be to explore the participants' beliefs and attitudes towards variables such as consulting primary care physicians, serum uric acid levels, treatment modalities, co-morbidities including other musculoskeletal problems and how they may influence their quality of life. The overall aim will be to identify the factors that participants (patients) consider as having the most important influence on their HRQoL.

The interview will also provide an opportunity to consult the participants regarding factors which they think should be taken into account by health care practitioners when treating gout, in order to improve treatment and potentially HRQoL.

Participants will be sent a letter of invitation, and PIS outlining the details of the interview process and reimbursement for their travel to the centre, including if necessary, pre-paid taxi. Participants will be asked to telephone the ARUKPCC if they are interested in taking part in order to book an appointment. Non-responders to this initial invitation letter will be sent a reminder invitation approximately two weeks later. Those willing to take part in the study will be booked into the next convenient interview group. Postal confirmation of the appointment will be made by letter and then by a reminder postcard shortly prior to the appointment. The postcard will be mailed in an envelope to maintain confidentiality about the nature of the appointment. The group interviews will be held at the ARUKPCC. Each group will have approximately 5 participants. Prior to commencing the interview, the procedures outlined in the PIS (for focus group interview) will be discussed with each participant. Participants will be given the opportunity to ask questions. Written informed consent to take part in the study will be obtained from all participants.

Risks to participants and safeguards to be put in place

This is a survey questionnaire study of patients with gout and as a result we expect the risks of harm to participants to be negligible. No potential adverse effects to participants are anticipated as a result of answering the questionnaire. There will be some burden with regards to the time it takes the participants to complete the questionnaires.

However the questionnaires follow a similar format to the questionnaires used previously by the ARUKPCC and have been designed to be as simple and clear to read as possible. At every point in the study the participants are reminded that their participation is voluntary and that they can withdraw from the study at any time without their care now or in the future being affected. Whilst the focus group interviews are designed to be brief and non intrusive, it is possible that a small number of participants may become distressed during the interviews. Any such distress is likely to be minor and short lasting. The researcher will be sensitive to this. Both the researcher and the patient will be aware that the interview can be terminated at any stage and audio file deleted. In the unlikely event of responses raising significant concerns, the researcher will be able to contact the GP in the first instance.

Follow-up *(Provide details of follow-up procedures and time points, if appropriate)*

Phase 4, 5, 6 and 7: Follow-up at 6, 12, 24 and 36 months

Follow-up surveys will be mailed at 6, 12, 24 and 36 months to all participants in phase 1 (baseline) who consented to further contact. The focus of follow-up will be clinical

(pain/disability severity) change and possible determinants of this. In addition to information about clinical change, the questionnaire will also include repeat measures of lifestyle, general health (including generic measures of physical function), psycho-social factors, co-morbidity and questions concerning the presence, duration, nature, severity, and impact of gout pain. Non-responders to the questionnaire will be sent a reminder postcard after two weeks. Those who do not respond to the reminder postcard will be sent a repeat questionnaire, PIS and a further covering letter four weeks after the initial mailing. The Primary Care Research Network team members will screen the mailing lists (prior to mailing) for patient deaths and departures from the practice to ensure that patients are not inappropriately contacted.

Outcome Measures (if appropriate)

Primary Outcome (A58 of IRAS form)

1. Gout related QOL will be measured using the Gout Impact Scale (GIS)
2. Physical functioning will be assessed via the Short Form 36 (SF36) physical function subscale (PF10) and the Health Assessment Questionnaire Disability Index (HAQ-DI).
3. The prevalence of chronic foot problems in gout over 3 years measured in terms of:
 - a) Foot pain – presence and location
 - b) Foot related disability – The Manchester Foot Pain and Disability Index (Manchester FPDl)
4. Anxiety and depression measured via the Generalised Anxiety and Disorder scale (GAD) as well as the Patient Health Questionnaire (PHQ-9).
5. The impact of gout on work and healthcare utilisation.

Secondary Outcome(s) (A59 of IRAS form)

Has a statistician or an advisor given an opinion about the statistical or methodological aspects and design of the research? (A57 of IRAS form) **Yes / No**

If YES, give the name and contact details:

Dr S Muller
Research Associate in Clinical Epidemiology
Arthritis Research UK Primary Care Centre
Primary Care Sciences
Keele University
Staffordshire
ST5 5BG
Email: s.muller@cphc.keele.ac.uk

If NO, then give reason why not:

Has the size of the study been informed by a formal statistical power calculation? **Yes / No / N/A**

If YES, indicate the basis upon which this was done, giving sufficient information to allow the replication of the calculation (A60 of IRAS form)

Disease specific HRQOL scores will be recorded using the Gout Impact Scale at baseline, 6, 12, 24 and 36 months. In order to use the information recorded at all five points, a sample size of 882 would allow a smallest meaningful difference in HRQOL of 0.2 standard deviation units to be detected between two groups (441 subjects per group) defined in terms of frequency of gout attacks (<2 attacks, ≥2 attacks per year) using a linear mixed model (significance 0.05, power 90%, autocorrelation 0.8) (22). Allowing for 70% response at baseline and 30% drop out over the follow-up period would require 1800 people with gout to be contacted at baseline.

If NO, explain how the size of the study was determined and why a formal sample size calculation is not required

If N/A, please explain

Describe the proposed methods of analysis (identifying specific procedures in the case of statistical analysis or analytical methods in the case of qualitative research) (A63 of IRAS form)

Data from the self completed questionnaire and general practice medical records will be analysed as follows:

- Descriptive account of flow of participants: eligible, mailed, responded, consented and followed up
- Age, gender and neighbourhood deprivation scores will be compared between baseline responders and non responders.
- Simple descriptive statistics will be used to describe the baseline characteristics of the study population, for example demographics, anthropometrics, gout duration, gout attack frequency, physical function, psycho-social factors, co-morbidities, musculoskeletal pain, chronic foot problems (foot pain presence, location, related disability; hallux valgus) etc. The prevalence of poor HRQoL (%; 95% confidence interval) will be calculated for the study population and then compared between sub-groups defined according to age, gender, self-reported BMI and socio-economic status. Continuous variables will be compared using students' t-tests and categorical variables using chi-squared tests.
- Crude (unadjusted) odds ratio between poor HRQoL and potentially associated variables at baseline such as gout characteristics (frequency of gout attacks, disease duration), chronic foot problems (pain, hallux valgus), co-morbidities (hypertension, hyperlipidaemia, diabetes mellitus, renal disease, vascular disease, musculoskeletal pain), gout treatment (allopurinol) and psycho-social factors (anxiety, depression) will be calculated with 95% confidence intervals. Significant variables identified in univariate analysis will then be entered into a multiple logistic regression model with poor HRQoL as the dependent variable.
- Cox proportional hazards regression will be used to calculate relative risk (RR) (95% confidence interval) for factors predicting poor HRQoL and chronic foot problems prospectively over three years.
- Amongst those people free of chronic foot problems (foot pain presence, location, related disability; hallux valgus) at baseline, the frequency of onset of chronic foot problems at 3 years will be described.
- Amongst those people with chronic foot problems at baseline, the frequency of persistence and progression of those problems (foot pain presence, spread, severity, associated disability; hallux valgus) at 3 years will be described.
- Imputation techniques will be used to account for missing data or loss to follow-up.

Where will the analysis of the data from the study take place and by whom will it be undertaken? (A42 of IRAS form)

The data generated by the study will be analysed at the ARUKPCC by the core research team including the chief investigator, principal investigator and study statistician. All these staff work to robust data security measures and have explicit duties of confidentiality equivalent to the duties placed on NHS staff, written into their

employment contracts. The chief investigator and study statistician have responsibilities under the research governance requirements to ensure the integrity of the data and that correct procedures are followed in obtaining, storing, protecting, accessing and reporting patient based research data. Specific responsibilities include ensuring that the law (Data Protection Act 1998), relevant regulations (Caldicott, Section 60, Health and Social care Act, General Medical Council, other professional bodies and the Medical Research Council guidelines on confidentiality and use of patient data, Research Governance Framework) and any other good practice guidelines are followed at all times. Only the relevant members of the research team will have access to the research data and this information will also be kept on the centre's central network drive. No information on patients' details or research data will be stored on personal computer hard drives, laptops, disks or other means where data could be transferred.

Participants' contact details will be erased 3 months after the final mailing. There are secure physical storage arrangements for the hard copy data at the centre within lockable filing cabinets. In addition, any hard copy research data that has been printed for checking will be destroyed by shredding. The centre also operates a key code entry system to ensure only appropriate persons are within the building.

Study Timetable

Start Date: 01/03/2012 **End date:** 31/12/2015
Duration: 3 years
Has funding for this project been secured? Yes / currently being sought / No
If yes or being sought, please provide details: Funded by the Arthritis Research UK Primary Care Centre. In addition Principal Investigator has been awarded funding for a PhD fellowship by the National School of Primary Care Research (NSPCR).

STATUS of STUDY (please indicate which)					
Student Project	<input checked="" type="checkbox"/>	Pilot study*		Full study	<input checked="" type="checkbox"/>

10 PROPOSED EXTERNAL INDEPENDENT REVIEWERS

11

12 For full projects, all applicants must provide names and e-mail addresses of three external independent reviewers (external to North Staffordshire). The Committee member reviewing the project may choose to send the project to one of your external reviewers, together with an external reviewer of their own choice.

13 For student or pilot research projects, all applicants are requested to provide the names of three external reviewers, as for full projects. Although these projects will normally only be reviewed by the Committee, judgment will be made by the Committee member if the project also requires external peer review.

- 1) Name: Dr Adrian Jones
E-mail: adrian.jones@nuh.nhs.uk
Organisation: Nottingham University Hospitals NHS Foundation Trust
Relationship between applicant and reviewer: Formerly chief investigator's supervising consultant
- 2) Name: Dr Adrian Pendleton
E-mail: a.pendleton@ntlworld.com
Organisation: Musgrave Park Hospital, Belfast
Relationship between applicant and reviewer: Formerly chief investigator's supervising consultant
- 3) Name: Prof Jim Woodburn
E-mail: jim.woodburn@gcal.ac.uk
Organisation: Glasgow Caledonian University
Relationship between applicant and reviewer: Nil

STUDENT PROJECTS

Supervisor's name and institutional address	Dr Edward Roddy Arthritis Research UK Primary Care Centre, Keele University, Staffordshire, ST5 5BG
Degree type and institution (if different from supervisor's)	PhD

Educational value of the project	This study will provide the student with experience of all aspects of undertaking a postal questionnaire survey including gaining
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	peer review, research ethics and NHS approvals, questionnaire design and the practical aspects of mailing; and data entry and cleaning. The student will also receive specific training concerning the conduct of focus group interviews and gain practical experience of undertaking and analysing such interviews. The student will learn and undertake basic statistical analysis under the supervision of members of the research team and will lead publications and conference presentations arising from the research.
Potential risks and safeguards to researcher	No risk envisaged
Supervision arrangements	Edward Roddy will be lead supervisor, with Christian Mallen (GP expertise) as the second supervisor. Further specialist support to the team will include Jane Richardson (qualitative methods expertise) and Sara Muller (statistical advisor). Formal face-to-face meetings between the student and supervisors will be held every month with the opportunity for informal meetings in-between as necessary. Progress meetings in accordance with University policy will be held between the supervisors and the student.
I can confirm that this project will be supervised in line with Research Governance requirements	<p>Supervisor signature</p> <p>.....</p> <p>Status of Supervisor</p> <p>.....</p>

Principal Investigator to obtain the necessary appropriate signatures	
AGREEMENT	SIGNATURE
<p>I confirm that the information submitted in this proposal is complete and correct and that this project will be conducted in accordance with Research Governance requirements.</p>	<p>Principal Investigator:Dr P Chandratre.....</p> <p>Signature:priyankachandratre.....</p>
<p>Having discussed this proposal with the applicant I confirm:-</p> <ul style="list-style-type: none"> that the research fits within the scientific programmes of the University / NHS Trust that if the proposal is approved all appropriate Research Governance requirements will be met. <p>If it is a joint project between the University and the NHS Trust, or involves both the University and the Trust, signatures must be obtained from BOTH organisations.</p>	<p><u>On behalf of the University</u></p> <p>Name:</p> <p>Signature:</p> <p>Post: Research Institute Director / Programme Director / Head of Department (please delete as appropriate)</p> <p><u>On behalf of the NHS Trust</u></p> <p>Name:</p> <p>Signature:</p> <p>Post: R&D Director / R&D Manager (please delete as appropriate)</p>
<p>I confirm that I have read this application and agree that if approved it will be accommodated and administered in the University / NHS Trust</p> <p>If it is a joint project between the University and the NHS Trust, or involves both the University and the Trust, signatures must be obtained</p>	<p><u>On behalf of the University</u></p> <p>Name:</p> <p>Signature:</p> <p>Post: Research Institute Director / Programme Director / Head of Department (please delete as appropriate)</p>

<p>from BOTH organisations.</p>	<p><u>On behalf of the NHS Trust</u> (to be signed off by an appropriate member of NHS Management)</p> <p>Name:</p> <p>Signature:</p> <p>Post:</p>
--	--

Once this application form has been completed and signed off as appropriate please send an electronic and hard copy to Nicola Leighton, Research Governance Officer, Research & Enterprise Services, Dorothy Hodgkin Building, Keele University, ST5 5BG, e-mail n.leighton@keele.ac.uk.

If you have any queries when completing the application form or would like further information on the independent peer review process, please contact Nicola Leighton on 01782 733306 n.leighton@keele.ac.uk.

***Definition of a pilot study**

A pilot study is one which acts as a precursor to a full study in order to determine the design and content of the full study. It can be used to evaluate and/or inform one or more aspects of the full study protocol. This may include:-

Methodology

Design:

Interview schedule

Data collection forms

Structure of questions

Selection of appropriate primary and secondary outcome measures

Recruitment:

Recruitment and consent

Statistical:

Power calculations of sample size

Randomisation process

Estimation of magnitude of effect of intervention

Acceptability

Likely acceptability of interventions and/or other procedures in the research process

Feasibility

Assess deliverability

Identification of unanticipated concerns

General issues:

Acquiring data for grant submission

Health and safety

On occasions, the pilot and full study may be presented as one application, but usually it is advisable to submit the pilot study for approval prior to consideration of the full study. If relevant, pilot studies may require power calculations and statistical analyses

Appendix 14: Peer reviewed research protocol



Keele University



Providing answers today and tomorrow

Peer Review Protocol

Prospective observational
cohort study of health
related quality of life,
chronic foot problems and
their determinants in gout

Dr Priyanka Chandratre (*Clinical research training fellow*)

Dr Edward Roddy (*Chief Investigator and research supervisor*)

Prof Christian Mallen (*Research supervisor*)

Dr Jane Richardson (*Qualitative research supervisor*)

Prof Keith Rome (*International collaborator and podiatry advisor, AUT University, Auckland, New Zealand*)

Introduction

Gout is the most prevalent inflammatory arthropathy, affecting around 1.4% of the adult population in the UK (1). It is caused by monosodium urate (MSU) crystal deposition in and around joints once the physiological saturation threshold in body tissues for uric acid is exceeded. The most commonly affected joints are the 1st metatarsophalangeal joint (MTPJ), mid foot and ankle. The first acute attack affects the first MTPJ in 56-78% of the patients with 90% having acute gout of the great toe at some point in their disease course (2). Gout also associates with hallux valgus deformity as well as chronic pain in the great toe (2). One further small hospital-based study has shown more frequent gait impairment and foot-related functional problems in gout than controls (3). With the exception of these two studies, there is little evidence from primary care about the potential long term consequences of gout as far as foot problems are concerned. Gout is an important condition not only because it is an excruciatingly painful acute arthropathy but also because of its associations with chronic disease states such as metabolic syndrome, osteoarthritis and renal and cardio-vascular morbidity (4).

In the face of such significant associated disorders, it is often difficult to attribute disability or diminished lifestyle to gout. This may be an explanation for the relatively sparse literature available around health related quality of life (HRQoL) and disability in gout patients (5). Most studies to date have had limitations such as small samples, cross sectional design and the use of generic instruments (which predate the disease specific Gout Impact Scale (GIS)) to measure HRQoL (6). Little is known about the changes in HRQoL in gout patients due to the lack of longitudinal follow up. However, severe chronic gout, through its frequency and severity of episodes and recurrent pain, may have a great impact on patients HRQoL. These symptoms, which may affect the patient's emotional, social and physical functioning, result in significant disability. Factors directly related to gout symptoms, as well as those related to disease complications and adverse effects of gout treatment, all potentially contribute to impaired HRQoL. Cross-sectional epidemiological studies in primary care have also shown that gout has an independent association with impaired HRQoL, particularly affecting the physical domain, after adjustments for co-morbidities such as osteoarthritis and vascular disease (7, 8). This finding is not unique - there are other studies emphasising the significant effect of 'treatment

failure' gout within a hospital-based gout cohort on patient HRQoL and disability, especially in the realm of physical functioning (5). In a 52 week prospective observational study, although co-morbidities contributed to impaired HRQoL, the scores were substantially lower than for the normative US adult male population, even for subjects who did not have any other illness (5). The same multi-centre prospective study demonstrated that the patients' perception of disease severity correlated more closely with HRQoL than the physicians' assessment of disease severity. Patients and healthcare providers often have different priorities as far as the optimal management of gout is concerned (9). A cross sectional qualitative study assessing the views of patients and physicians highlighted marked differences in what is important to each group. Whilst the physicians regarded pharmacological treatment of gout to be effective, most patients discontinued treatment due to adverse or no positive effects, paradoxical flares and financial constraints. Patients also expressed lack of understanding of gout, a disease physicians felt was easy to comprehend for the patients. Health care providers felt they had adequate training to educate patients about disease self management, an area patients wanted to know more about. A recent qualitative study (10) on the impact of gout highlighted the lack of understanding and the stigma associated with this condition which often leads to under reporting of symptoms. This in turn can lead to suboptimal treatment despite disease severity.

These findings are not surprising given that, until recently, there has not been much published work on the implications of gout in terms of morbidity and mortality as well as associated healthcare utilisation and costs (11). The majority of gout is dealt with within the primary care setting, yet most of the research to date has taken place in secondary care which may deal with more complex and atypical presentations including those who have failed to respond to or not tolerated standard therapies. Therefore the applicability of such data is questionable in the wider setting of the community. There are several issues around the management of gout which need better understanding through robust research. At present it is estimated that only 30% of patients take definitive treatment (e.g. allopurinol) for gout in primary care (12, 13). This is despite recommendations from international guideline groups which advocate the use of urate-lowering therapies (ULTs) such as allopurinol to lower uric

acid levels, shrink tophi and prevent acute attacks of gout (14, 15). There is no clear explanation for the discrepancy between the recommended and actual treatment of gout, although the potential for drug toxicity, interactions and polypharmacy associated with co-morbidity might reduce uptake of long-term treatment. International treatment recommendations suggest that patients experiencing two or more attacks in a 12-month period should be offered ULT but this recommendation is based upon expert consensus rather than empirical research evidence (15, 16). Improving understanding of which factors predict outcome would help substantiate indications for ULT and identification of patients at which this should be targeted. Hence there is a need for a well-designed and conducted prospective observational cohort study in primary care which incorporates patient reported outcomes (PRO) to assess long term outcome and consequences of gout, focusing particularly on HRQoL and foot problems.

Objectives of the study

The main objectives of the study are:

1. To estimate the prevalence of poor HRQoL in patients with gout and its distribution by demographic, socio-economic and anthropometric characteristics (cohort study – baseline data).
2. Describe the prevalence, onset, persistence and progression of chronic foot problems in gout over 3 years (cohort study – baseline and follow-up data).
3. To examine:
 - a) Cross-sectional associations between poor HRQoL and frequency of gout attacks, chronic foot problems, co-morbidities, gout treatment, and psychosocial factors in gout (cohort study – baseline data).
 - b) Change in HRQoL in gout over 3 years and determine which of the associated factors may predict deterioration (cohort study – baseline and follow-up data).
4. To explore patient experience of gout focusing on impact of gout and its treatment on HRQoL (cohort study – nested focus group interviews).

Methods /design

Design

Primary care-based prospective cohort study with follow-up focus group interviews.

Sampling frame

All adults (aged >18 years) registered with 30 general practices in the West Midlands who have had:

- A consultation for gout in the preceding two years or,
- Prescription for colchicine or allopurinol in the preceding two years.

Patient eligibility

Inclusion criteria

- Registered with the participating general practice during the study
- Read code consultation for gout or prescription for colchicine or allopurinol during the preceding two years
- Provided written informed consent for participation in the study

Exclusion criteria

- Under 18 years of age
- Vulnerable groups – e.g. significant cognitive impairment, severe enduring mental illness, active malignancy or other terminal illness.

Data collection time points

- Phase 1: Baseline postal questionnaire
- Phase 2: Review of general practice medical records
- Phase 3: Focus group interviews (nested purposive sample)
- Phase 4: Follow-up mailed survey at 6 months
- Phase 5: Follow-up mailed survey at 12 months
- Phase 6: Follow-up mailed survey at 24 months
- Phase 7: Follow-up mailed survey at 36 months

Phase 1: baseline postal questionnaire survey

Patient identification

All potentially eligible patients registered within the participating general practices will be identified through standard Read codes used for gout or prescription of colchicine or allopurinol. The following Read codes are used by the Arthritis Research UK Primary Care Centre (ARUKPCC);

Code	Term
C34	Gout
N023	Gouty arthritis
EGTON 227	Gout NOS
OX2740G	Gout Acute /ox
1443	H/O: gout
EMISR4QG01	Gouty tophi + Gout NOS
2D52	O/E - auricle of ear - tophi
669	Gout monitoring

Staff from the Keele Primary Care Research Network will conduct a one off electronic search of the primary care records in participating practices to identify patients with a consultation for gout or a prescription for colchicine or allopurinol within the last two years. The names and contact details of the eligible patients will be stored in a password protected mailing database and held on the university's firewall and password protected server. No other information from the patients' primary care records will be accessed or stored unless and until informed written consent to do so is obtained from the patient. The Primary Care Research Network team members will screen the mailing lists (prior to mailing) for patient deaths and departures from the practice to ensure that patients are not inappropriately contacted. The lead general practitioner (GP) at each practice will be invited to identify potentially vulnerable patients to be excluded.

Initiating patient contact

All eligible patients will be sent a study pack from their general practitioner (on general practice headed notepaper). This will contain a letter of invitation, participant information sheet (PIS), a pre-paid return envelope and a baseline self-administered questionnaire which will also include a consent form asking for consent:

- a) For further contact by post
- b) For review of their medical records

Potential participants will also be provided with a contact name and telephone number should they have any queries about the study. Patients will be informed that they are under no obligation to participate and that if they decline their normal clinical care will not be affected in any way. On return of the questionnaire the response is recorded against a unique patient number – this will include completed questionnaires, contact details, request to be excluded from the study and non responders. Participants returning their questionnaires with the consent sheet and those who wish to be excluded from the study (non-consenting responders) will be logged on the database so that no further reminders are sent to them. The mailing database will determine future mailings. By including the consent form with the

questionnaire we are hoping to avoid the wasteful exclusion of completed questionnaires but incomplete consent forms thereby preventing any adverse effects on data quality.

The questionnaire

The questionnaire will be divided into 7 main sections

- a) About gout symptoms and treatment
- b) The impact of gout on daily life
- c) General health (including co-morbidities and measures of physical function)
- d) Measures of anxiety and depression in gout patients
- e) Foot and other joint problems
- f) Occupational characteristics
- g) Socio-economic and demographic characteristics

Details of the conceptual domains, operational definitions and empirical measures are provided in Appendix 1. The completed baseline questionnaires will have the responses securely stored in the study database. This database will be used in cross-sectional analyses where appropriate.

Non-responders to mailed study pack

As per the ARUKPCC questionnaire mailing Standard Operating Procedure, non-responders are sent a reminder postcard at two weeks and a reminder letter with repeat baseline questionnaire two weeks later (4 weeks after the first questionnaire) (17). This approach maximises response without placing significant burden on patients. Those who fail to respond after all three baseline mailings will be assumed not to have consented to the study and will not be contacted again.

Data entry, coding, cleaning and storage

A specific study database will be created and tested using a set of dummy data first. Data entry will be performed by dedicated members of the administrative team as the completed questionnaires are returned. Although they are experienced in data

entry, specific training will be provided for this study. The principal investigator (PI) and study statistician will determine coding prior to data entry into the database which will provide coding options. Some standard codes (e.g. missing data (-9), not applicable (-88)) are used by the research centre and will also be utilised in this study. One in ten random questionnaires will be checked by a member of the study team for the purposes of quality assurance. This information is kept by the research support co-ordinator and study statistician. Only relevant members of the research team will have access to the database which is password protected. Requests for access to the data stored in this database must be made in writing, along with an analysis plan, to the PI. Questionnaires and consent sheets are securely stored in separate locations to protect the confidentiality of the patients.

Phase 2: Review of general practice medical records

All participants in Phase 1 who give permission for their GP records to be accessed will have their computerised medical records tagged by a member of the Primary Care Research Network. All consultations for the 24-months prior to study entry and then prospectively for the three-year study period will be identified. The practices participating in this study are fully computerised and undergo annual audits completed by the Primary Care Research Network to assess the quality and completeness of the data entry at the practices (18). All relevant gout related consultations or prescription for colchicine or allopurinol will be identified using search techniques based on Read codes and free text entries. Such searches have already been developed and successfully applied for foot and knee-related consultations in the Centre's cohorts (19-21). Full medical records of the consenting participants will be accessed for information regarding co-morbidities, other musculoskeletal problems, repeat consultations in primary care for gout (clinician recorded diagnosis mapped to standard Read code morbidity codes), prescription patterns and referral to secondary care. All sensitive data (name, contact details) will be removed from the medical records and the consultation data will be linked to the survey data by unique survey identifier.

Phase 3: Qualitative focus group interviews

Phase 3 will consist of exploratory qualitative focus group interviews to investigate the previously unobserved factors that patients perceive as important outcomes of their gout treatment. By using an inductive qualitative strategy we hope to cover aspects of patient experience of gout treatment not considered previously. Focus groups will encourage participants to discuss and share their individual experiences, thereby producing a more comprehensive and unconstrained account of patients' perceptions, thoughts and beliefs about the treatment of gout. In addition the group dynamics will encourage participants to question and reflect on each other's responses, hence reducing interruption from the moderator.

Choice of participants

Drawing on the expertise of the research team a purposive sampling framework will be developed to identify participants encompassing a broad range of demographic and disease characteristics from the prospective observational cohort of gout patients. A sub-sample of 20 participants will be invited to one of four focus group interviews (each group consisting of 5 participants) initially. The group interviews will be held at the ARUKPCC or at the GP practices if facilities to do so are available. Participants will be sent a letter of invitation, and PIS outlining the details of the interview process and reimbursement for their travel to the centre (or GP practice as appropriate), including if necessary, pre-paid taxi. Participants will be asked to return a form (sent with the letter of invitation) to the ARUKPCC using a pre-paid return envelope, if they are interested in taking part in order to book an appointment. Non-responders to this initial invitation letter will be sent a reminder invitation approximately two weeks later. Those willing to take part in the study will be booked into the next convenient interview group. Postal confirmation of the appointment will be made by letter and then by a reminder postcard shortly prior to the appointment. The postcard will be mailed in an envelope to maintain confidentiality about the nature of the appointment. Prior to commencing the interview, the procedures outlined in the PIS (for focus group interview) will be discussed with each participant. Participants will be given the opportunity to ask questions. Written informed consent to take part in the study will be obtained from all participants.

Interview schedule

The key question of interest in the interview schedule will be:

“What do you expect your gout treatment to achieve or improve?”

If prompts are needed the moderator can also ask about the following:

- Satisfaction with treatments and their effectiveness
- Subjective symptoms that describe patients' perception of ill health in the context of their overall life situation, both physical and psycho-social

Finally the moderator will provide a closing summary, invite any additional points for discussion and clarify any misinterpretations should they arise.

Analysis

The interviews will be carried out by a single moderator who has specific training of qualitative research methods with a particular emphasis on focus groups. The interviews will be tape recorded and transcribed verbatim. Data analysis will be conducted using thematic analysis. The moderator will read the data transcripts carefully and highlight discreet words and sentences that form the basis of key concepts and codes relevant to aspects of gout treatment. All patient responses will be categorised by concepts (or codes) into provisional themes and reviewed across patients for each focus group. To enhance the scientific rigour a second researcher will analyse the transcripts to identify the emerging concepts and themes. It is likely that a second researcher from a different background will identify different concepts and themes. A discussion between the two researchers will help to clarify and consolidate themes and concepts.

Phase 4, 5, 6 and 7: Follow-up at 6, 12, 24 and 36 months

Follow-up surveys will be mailed at 6, 12, 24 and 36 months to all participants in phase 1 who consented to further contact. The focus of follow-up will be clinical (pain/disability severity) change and possible determinants of this. Those participants who agree to further contact at baseline (phase 1) will be mailed a further questionnaire at each follow-up stage. In addition to information about clinical change, the questionnaire will also include repeat measures of lifestyle, general health (including generic measures of physical function), psycho-social factors, co-morbidity and questions concerning the presence, duration, nature, severity, and impact of gout pain. Non-responders to the questionnaire will be sent a reminder postcard after two weeks. Those who do not respond to the reminder postcard will be sent a repeat questionnaire, PIS and a further covering letter four weeks after the initial mailing. The Primary Care Research Network team members will screen the mailing lists (prior to mailing) for patient deaths and departures from the practice to ensure that patients are not inappropriately contacted. The study procedure is summarised in a flow chart in Appendix 2.

Sample size

Disease specific HRQOL scores will be recorded using the Gout Impact Scale at baseline, 6, 12, 24 and 36 months. In order to use the information recorded at all five points, a sample size of 882 would allow a smallest meaningful difference in HRQOL of 0.2 standard deviation units to be detected between two groups (441 subjects per group) defined in terms of frequency of gout attacks (<2 attacks, ≥ 2 attacks per year) using a linear mixed model (significance 0.05, power 90%, autocorrelation 0.8) (22). Allowing for 70% response at baseline and 30% drop out over the follow-up period would require 1800 people with gout to be contacted at baseline.

Statistical analysis

Data from the self completed questionnaire and general practice medical records will be analysed as follows:

- Descriptive account of flow of participants: eligible, mailed, responded, consented and followed up

Study Protocol, version 1.0, dated 15/02/12

- Age, gender and neighbourhood deprivation scores will be compared between baseline responders and non responders.
- Simple descriptive statistics will be used to describe the baseline characteristics of the study population, for example demographics, anthropometrics, gout duration, gout attack frequency, physical function, psycho-social factors, co-morbidities, musculoskeletal pain, chronic foot problems (foot pain presence, location, related disability; hallux valgus) etc. The prevalence of poor HRQoL (% , 95% confidence interval) will be calculated for the study population and then compared between sub-groups defined according to age, gender, self-reported BMI and socio-economic status. Continuous variables will be compared using students' t-tests and categorical variables using chi-squared tests.
- Crude (unadjusted) odds ratio between poor HRQoL and potentially associated variables at baseline such as gout characteristics (frequency of gout attacks, disease duration), chronic foot problems (pain, hallux valgus), co-morbidities (hypertension, hyperlipidaemia, diabetes mellitus, renal disease, vascular disease, musculoskeletal pain), gout treatment (allopurinol) and psycho-social factors (anxiety, depression) will be calculated with 95% confidence intervals. Significant variables identified in univariate analysis will then be entered into a multiple logistic regression model with poor HRQoL as the dependent variable.
- Cox proportional hazards regression will be used to calculate relative risk (RR) (95% confidence interval) for factors predicting poor HRQoL and chronic foot problems prospectively over three years.
- Amongst those people free of chronic foot problems (foot pain presence, location, related disability; hallux valgus) at baseline, the frequency of onset of chronic foot problems at 3 years will be described.
- Amongst those people with chronic foot problems at baseline, the frequency of persistence and progression of those problems (foot pain presence,

spread, severity, associated disability; hallux valgus) at 3 years will be described.

- Imputation techniques will be used to account for missing data or loss to follow up.

APPENDIX 1

QUESTIONNAIRE ITEMS

Version 1.0 dated 15/02/12

Conceptual domain	Operational definition	Empirical measure	Number of items	Time point
Section A: About Gout				
Gout frequency	No. of attacks in the last 12 months/since last contact	Numerical rating scale 0-≥5	1	All
Age at diagnosis	Age in years	Numerical free text box	1	BL
Acute attack of gout	Acute episode at time of questionnaire	Yes/ No	1	All
Allopurinol	Reported use of allopurinol	Yes/No	1	All
	Current daily dose of allopurinol	Nine daily dose options: 50mg-900mg	1	All
Section B: How gout affects your life				
Gout concern, wellbeing, productivity, convenience and satisfaction	Gout Impact Scale (6)	5-item Likert scale	18	All
Illness perception	Illness perception questionnaire (23)	5-item Likert scale	4	BL, 12 months, 36 months
Section C: General Health				

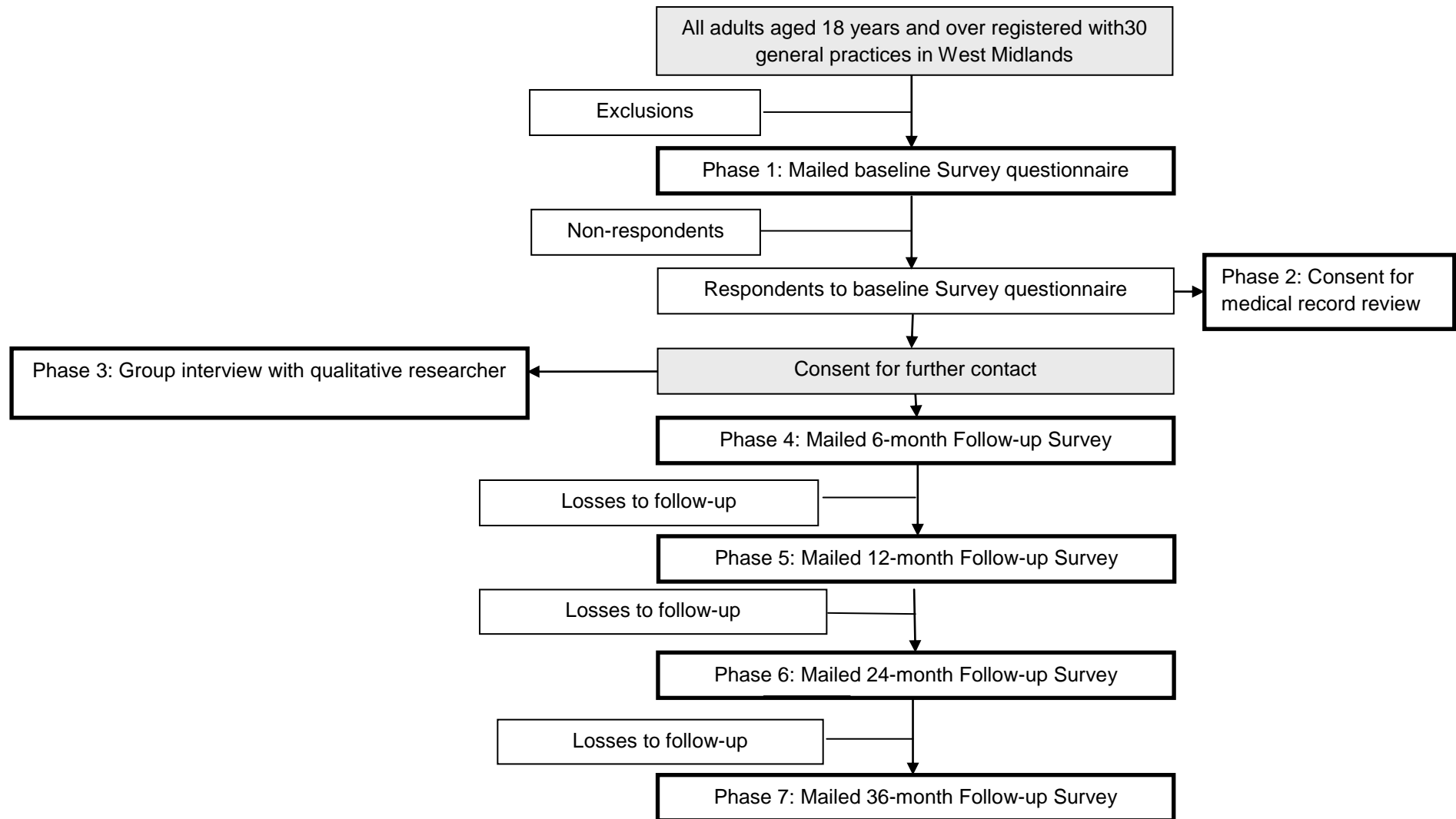
Physical function	SF36 Physical function sub-scale (PF10) (24)	3-item Likert scale	10	All
	Health Assessment Questionnaire Disability Index (25)	4-item Likert scale	17	All
Co-morbidities	Diabetes mellitus, Renal failure and calculi, CVA and TIA, IHD, hyperlipidaemia	Yes / No	9	BL
Section D: How you feel				
Anxiety and depression	Patient health questionnaire (PHQ 9) (26) Generalised anxiety disorder questionnaire (GAD) (27)	4 point Likert scale	16	BL, 12 months, 36 months
Section E: Foot and other joint problems				
Hallux valgus	Self-completed line drawings (28)	5 line-drawings for each foot depicting increasing severity of hallux valgus	2	BL, 12 months, 36 months
Pain	Pain in the hands, hips, knees and feet in the last year Location of body pain in last 4 weeks	Yes/No	4	BL, 12 months, 36 months
		Self-completed body manikin (29, 30)	1	BL, 12 months, 36 months
Foot pain	Foot pain, aching, stiffness in last month (31)	Frequency on 5-point Likert scale	1	BL, 12 months, 36 months
Foot pain location	Location of foot pain in last four weeks	Self-completed foot manikin (32)	1	BL, 12 months, 36 months

Foot function	Manchester Foot Pain and Disability Index (33)	Frequency on 3-point likert scale	17	BL, 12 months, 36 months
Consultation for foot problems	Consultation with GP, physiotherapy, podiatry, chiropody since last 12 months/since last contact	Yes/No	4	BL, 12 months, 36 months
Section F: Work				
Occupational characteristics	Current employment status	11-response options	1	BL, 12 months, 36 months
	Work absence during last 6 months due to joint/back problems	Yes/No	1	BL, 12 months, 36 months
	Ability to do usual job	5-response options	1	BL, 12 months, 36 months
Section G: Demographic/socioeconomic characteristics				
Date of birth and gender	Date of birth and gender	Date of birth, male/female	2	BL
Anthropometric characteristics	Height	Metres or feet/inches	1	All
	Weight	Kilogram or stones/pounds	1	All
Marital status	Marital status	6-response options	1	BL
Living alone	Living alone	Yes/No	1	BL
Adequacy of income	Adequacy of income	4-response options	1	BL

Education	Higher education	Yes/No	1	BL
Ethnicity	Ethnicity	6-response options	1	BL
Life-style-characteristics	Frequency of alcohol consumption	6-response options	1	BL
	Weekly amount of beer/spirits/wine consumed	Free-text	1	BL
	Smoking status	3-response options	1	BL

APPENDIX 2

FLOWCHART OF STUDY PROCEDURE



APPENDIX 3

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Appendix 15: Approval from independent peer review committee



24 February 2012

Dr Priyanka Chandratre
Arthritis Research UK Primary Care Centre
Primary Care Sciences
Medical School
Keele University

Dear Dr Chandratre

Prospective observational cohort study of health related quality of life and chronic foot problems and their determinants in gout

As you know the above project was initially awarded a grade 2 but following assessment of your response to the issues raised the project now has received final approval from the Independent Peer Review Committee and can be submitted for ethical approval.

The reviewer assessing your response is happy to award the project a grade 1 but would like to draw your attention to the following point:-

- If you remove a section of a transcript from a focus group it really invalidates the data before and after this section, as one of the prime reasons for using a focus group is that the group generates the data. Such that what is said before stimulates and reflects what is said next and so on. The researchers may wish to say that they will not use the data as a quotation in published work – but this should be covered in the standard consent form anyway

I am attaching a letter addressed to the Chair of the NHS REC along with the original peer review comments which you can enclose with your NHS REC application.

Management approval

You should arrange for all relevant NHS care organisations to be notified that the research will be taking place, and provide a copy of the REC application, the protocol and this letter.

All researchers and research collaborators who will be participating in the research must obtain management approval from the relevant care organisation before commencing any research procedures. Where a substantive contract is not held with the care organisation, it may be necessary for an honorary contract to be issued before approval for the research can be given.



Clinical trial of a medicinal product

Please remember that, if your project is a clinical trial of a medicinal product, MHRA approval is required. You must submit a request for a clinical trial authorisation under the Medicines for Human Use (Clinical Trials) Regulations 2004. Further details can be found at

<http://www.mhra.gov.uk/home/groups/lunit1/documents/websiteresources/con2022633.pdf>

If you have any queries, please do not hesitate to contact Nicola Leighton on 01782 733306.

Yours sincerely

A handwritten signature in black ink, appearing to read 'PMS O'Brien', with a long horizontal line extending to the right.

Professor PMS O'Brien
Chair – Independent Peer Review Committee

Enc



K E E L E
UNIVERSITY
24 February 2012

**ACADEMIC SERVICES DIRECTORATE
RESEARCH AND ENTERPRISE SERVICES**

Chair
NHS Research Ethics Committee

Dear Sir/Madam

Investigator : Dr Priyanka Chandratre

Name of study : Prospective observational cohort study of health related quality of life and chronic foot problems and their determinants in gout

Please find attached the peer review of the above project.

The project was initially awarded a grade 2 (minor revisions were required)

The Independent Peer Review Committee are satisfied that the issues raised have been answered and that the project can now be awarded a grade 1 and therefore can proceed for ethical review without any revision.

We have informed the applicant that although this project has been deemed appropriate based on scientific merit, they wish to incorporate the reviewer's constructive comments to strengthen their protocol.

We have also stressed to the applicant that the Independent Peer Review Committee is NOT linked to or a Sub-Committee of the Local Research Ethics Committee and that you may identify ethical issues of your own.

Yours sincerely

Professor PMS O'Brien
Chair – Independent Peer Review Committee



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PEER REVIEWER'S PROFORMA

Research Project Details	
Project title	Prospective observational cohort study of health related quality of life and chronic foot problems and their determinants in gout
Name of principal investigator	Dr. Priyanka Chandratre
Institution of principal investigator	Keele University

The important or relevance of the problem to be addressed in relation to either or both of:

- a) The particular field of research as a whole

The area of gout in primary care seems to have been under-researched in primary care and this work proposes to address some of the gaps in the knowledge base.

- b) The value of this research for health or social care

Greater emphasis is now being placed on early diagnosis and prevention of long-term disability so it would seem appropriate to explore factors that may inform management of this inflammatory arthropathy from both a pathophysiological and the patient's perspective.

The quality and relevance of the background information provided

Good.

The background literature identifies that there is limited research in this area. Additionally, what has been done has either been undertaken in the hospital setting, not utilised more current and appropriate outcome measures, or the short follow up timeframe of such studies is not adequate to inform the management of a chronic condition. This has thereby limited the understanding of this condition.

Design, methods and strengths and weakness of the proposed plan of investigation

This is an observational epidemiological study using self-completion health survey questionnaires over a period of 3 years.- Pilot study

The study appears to be a longitudinal survey using a questionnaire incorporating validated health questionnaires but with an additional 'qualitative' element.

The phases 1, 2, 4, 5, 6 and 7 are described well and seem logical such that the study should fulfil objectives 1-3.

However the qualitative element, Phase 3, designed, to meet objective 4; "To explore patient experience of gout focusing on impact of gout and its treatment on HRQoL (cohort study – nested focus group interviews)." raises some issues.

If an understanding of the impact of gout and quality of life in any meaningful way is the objective of this phase it is unlikely to be achieved through this data collection method. The choice of topics for the focus groups is also not clear – they seem to relate to rather medical or clinical aspects of the participants' condition, and it is unclear why the focus is specifically on these issues, rather than on those that relate more directly to the patient's experience of health-related quality of life. It may be better to gain more depth knowledge of the patients' experiences of gout by undertaking individual interviews with various patients over the whole three years or to follow several patients over the study with a series of interviews.

As it stands, the focus groups appear to have been appended to the main study, rather than being an integrated means of addressing the main study objectives.

Has consideration been given to other locations to conduct these focus groups to maximise attendance? Additionally, caution and greater thought needs to be given to the statement "the interview can be terminated at any stage and audio file deleted" this will very difficult if one person wishes to stop a focus group and the data from *all* participants will be lost.

The quality of analysis provided (statistical or qualitative, as appropriate)

Statistical advice has been sought.

The analysis of data from the questionnaires and medical records is well described and seems appropriate.

There is no indication of how the data from the focus groups will be analysed or used.
Is it intended to check the rigour and appropriateness of the analysis, e.g. by another investigator reviewing some of the analysed text?

The capacity and expertise of the research team in the context of the proposed study

The members of the team offer expertise in the areas of primary care, rheumatology and methods.

Appropriateness of resource requirements

General feedback (indicate major areas where changes will be required, indicate whether any weaknesses indicated in any of the above categories are major or minor areas of concern)

The questionnaire survey alone offers an opportunity to address an area of limited knowledge about a chronic condition.

The major concern is Phase 3; the role and value of this phase in this *specific* project should be reconsidered. If a qualitative element is to be included greater thought needs to be given to its purpose, and the process of both data collection and data analysis.

Assessment of Merit

Grading	Description	Please tick
1	Proceed without any revision. Project may be submitted for appropriate NHS/University approval and then to either the Local or the Multi-Centre Research Ethics Committee.	
2	Minor amendments or Further information required. Revise project according to reviewer(s) recommendations. Document to be checked by Internal Committee Member prior to Chairman's approval to proceed.	√
3	Complete major revision required. Principal Investigator to discuss outcome with Centre/Programme Director and agree plan to complete substantive revision of the project (with support as agreed). Resubmission will need to be reviewed and approved by Internal Committee Member, prior to Chairman's approval to proceed.	
4	Reject on the basis that the project has major scientific flaws	

**Appendix 16: Approval from North West Liverpool East Local Research
Ethics Committee (REC reference number: 12/NW/0297**

NRES Committee North West - Liverpool East

HRA NRES Centre North West
Barlow House
3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7832
Facsimile: 0161 625 7299

30 April 2012

Dr Edward Roddy
Clinical Senior Lecturer in Rheumatology/ Honorary Consultant Rheumatologist
Keele University
Arthritis Research UK Primary Care Centre
Keele University
Staffordshire
ST5 5BG

Dear Dr Roddy

Study title: Prospective observational cohort study of health related quality of life and chronic foot problems and their determinants in gout.
REC reference: 12/NW/0297
Protocol number: Protocol Number 1.0

The Research Ethics Committee reviewed the above application at the meeting held on 19 April 2012. Thank you for attending with Dr Priyanka Chandratre to discuss the study.

Ethical opinion

The Committee welcomed you both to the meeting and thanked you for what they had found to be a very well-written study.

The Committee firstly asked why this study had not been submitted through the Proportionate Review service. Neither of you knew the reason.

The Committee had noted that in the Participant Information Sheet it was stated that questionnaires would be kept for 20 years and suggested that they be destroyed at the end of the study. You both agreed.

The Committee felt that there was a possibility that participants could be distressed and asked how this would be managed. Dr Chandratre explained that it is not intended that the participants would be distressed but if they were she would use her training to manage the situation. She would offer the participant the chance to take a break and step outside the room. She would ask if they still wanted their data to be included and would remove it if not. If the distress was longer term she would suggest they contact their GP. You emphasised that the questionnaire is not particularly likely to distress the participant.

The Committee made reference to question 1.i. in section D of the Gout Study Questionnaire which asks how often a person has had *'thoughts that you would be better off dead or of*

hurting yourself in some way. The Committee felt that questions such as this would potentially distress participants. You explained that the questionnaire is validated and this is just a single question.

The Committee suggested that questions such as this may potentially trigger pre-existing distress. It was suggested that contact details for an alternative source of support such as a support group or charity were given. You both agreed.

The Committee asked about the GP practices to be involved in the study and how they would be notified as they had not seen a letter included with the application. You explained that the GP practices are already signed up to the research network.

The Committee asked if they would be including participants on the new gout drug Febuxostat. You explained that they would not. The prescription rate for this drug is very low.

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see “Conditions of the favourable opinion” below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission (“R&D approval”) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation’s role in the study is limited to identifying and referring potential participants to research sites (“participant identification centre”), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

The Committee gave a favourable opinion of the application (with additional conditions as follows):

- Written clarification that questionnaires and tapes would be destroyed at the end of the study and not after 20 years should be provided. This should be amended on page 2 of the Patient Information Sheets (questionnaires and interviews).
- A section should be included in the Patient Information Sheet (questionnaires) about the risks of participating in the study. Information should be included in this section about the possibility of becoming distressed during the study and what should be done in this situation. Information should be included about support groups or charities that could be contacted if available.
- The location of the interview should be given in the Patient Information Sheet (interviews).
- It should be made clear in the Patient Information Sheet (interviews) that if distressed the participant could leave the interview.
- The contact details for someone who could be contacted in the event of distress should also be given at the end of the questionnaire.
- The Consent Form should include the following standard paragraph: 'I understand that my medical notes and data collected during the study may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to the records'.

It is responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Confirmation should also be provided to host organisations together with relevant documentation

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Covering Letter from Edward Roddy		29 March 2012
REC application: 89315/309525/1/664		02 April 2012
Protocol	1.0	15 February 2012
Investigator CV Dr Edward Roddy		29 March 2012
Investigator CV Dr Priyanka Chandratre		29 March 2012
Investigator CV Professor Christian Mallen		05 April 2012
Investigator CV Jane Crompton Richardson		
Letter from Sponsor from Rhian Hughes		02 March 2012
Letter from Statistician from Dr Sara Muller		16 February 2012
Peer Review Report- Outcome letter and revisions made after initial review		24 February 2012
Letter to REC from Peer Review Committee from Professor PMS O'Brien		24 February 2012
GP Information Leaflet	1.0	15 February 2012
Letter of invitation to participant: Focus group interview	1.0	15 February 2012

appointment letter		
Letter of invitation to participant: invitation letter sent regarding the focus group interview		
Participant Information Sheet: for gout interview	1.0	15 February 2012
Participant Information Sheet: for the gout study	1.0	15 February 2012
Participant Consent Form: focus group interview	1.0	15 February 2012
Two week reminder letter for focus group interviews	1.0	15 February 2012
Covering letter sent with baseline questionnaire booklet	1.0	15 February 2012
Covering letter to be sent with 6 months follow up questionnaire booklet	1.0	15 February 2012
Covering letter to be sent with 12 months follow up questionnaire booklet	1.0	15 February 2012
Covering letter to be sent with 24 months follow up questionnaire booklet	1.0	15 February 2012
Covering letter to be sent with 36 months follow up questionnaire booklet	1.0	15 February 2012
Two week reminder postcard	1.0	15 February 2012
Two week reminder postcard sent after baseline questionnaire	1.0	15 February 2012
Reminder letter sent with repeat Questionnaire at week 4	1.0	15 February 2012
Reminder letter to be sent with repeat 6 months Questionnaire	1.0	15 February 2012
Reminder letter to be sent with repeat 12 months Questionnaire	1.0	15 February 2012
Reminder letter to be sent with repeat 2 years Questionnaire	1.0	15 February 2012
Reminder letter to be sent with repeat 3 years Questionnaire	1.0	15 February 2012
Focus Group reminder postcard	1.0	15 February 2012
Gout Study Questionnaire- baseline questionnaire booklet	1.0	15 February 2012
Gout Study Questionnaire- 6 months follow up questionnaire booklet	1.0	15 February 2012
Gout Study Questionnaire- 12 months follow up questionnaire booklet	1.0	15 February 2012
Gout Study Questionnaire- 2 years follow up questionnaire booklet	1.0	15 February 2012
Gout Study Questionnaire- 3 years follow up questionnaire booklet	1.0	15 February 2012
Evidence of insurance or indemnity from George Smith		21 July 2011

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document “After ethical review – guidance for researchers” gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback


You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

12/NW/0297	Please quote this number on all correspondence
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With the Committee’s best wishes for the success of this project

Yours sincerely



On behalf of
Mrs Jean Harkin
Chair

Email: helen.penistone@northwest.nhs.uk

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

“After ethical review – guidance for researchers”

Revised Approved docs. Table 2012.06.27

Copy to:

Dr Priyanka Chandratre
Arthritis Research UK Primary Care Centre
Keele University
Staffordshire
ST5 5BG

Rhian Hughes
Arthritis Research UK Primary Care Centre
Keele University
Keele
Staffordshire
ST5 5BG

Mrs Pam Devall
Stoke-on-Trent Primary Care Trust
NHS Stoke-on-Trent
4th Floor
Hide Street
Stoke-on-Trent
ST4 1NF

NRES Committee North West - Liverpool East

Attendance at Committee meeting on 19 April 2012

Committee Members:

<i>Name</i>	<i>Profession</i>	<i>Present</i>	<i>Notes</i>
Mr John Bridson	Clinical Ethicist	Yes	
Dr Zoe Edwards	Clinical Psychologist	Yes	
Mrs Jean Harkin	Chair / Solicitor	Yes	
Mrs Maureen Hendry	Pharmacist	Yes	
Mrs Glenys J Hunt	Alternate Vice Chair / Solicitor	Yes	
Mr Chris Irving	Biomedical Scientist	Yes	
Professor Ebrahim Khalil Naderali	Professor of Human Physiology	Yes	
Mr Alex Newgrosh	Quality Assurance Manager	Yes	
Professor Neil Pender	Professor of Orthodontics	Yes	
Miss Helen Penistone	Co-ordinator	Yes	
Mrs Jean Pownceby	Lay Member	Yes	
Dr Richard Sarginson	Consultant (Anaesthesia/PICU)	Yes	
Ms Karen Tripp	Research Governance Administrator	Yes	
Dr Peter Walton	Lay Member	Yes	

Appendix 17: Revisions submitted to REC

To,

8th May 2012

Mrs Jean Harkin

Chair of the NRES Committee North West – Liverpool East

HRA NRES Centre North West

Barlow House

3rd Floor

4 Minshull Street

Manchester M1 3DZ.

Reference: 12/NW/0297

Re: Prospective observational study of health related quality of life and chronic foot problems and their determinants in gout.

Dear Mrs Harkin,

Thank you for the comments provided by the 12/NW/0297 Research Ethics Committee (REC) which we read with great interest. We thank the panel members for the suggestions made. We have tried to address these issues as outlined below.

Written clarification that questionnaires and tapes would be destroyed at the end of the study and not after 20 years should be provided. This should be amended on page 2 of the Patient Information Sheets (questionnaires and interviews).

In keeping with the Medical Research Council's (MRC) policy of data storage, as outlined in section 7.1.2 of the '*Personal Information in Medical Research- Medical Research Council Ethics Series*', we plan to store anonymised data in the form of questionnaires and digitalised audio data (from Focus Group Interviews) along with the transcripts for twenty years. This is an acceptable length of time for data storage as per the MRC policy;

"MRC would expect that research records relating to clinical or public health studies should be maintained for twenty years, to allow adequate time for review, reappraisal, or further research, and to allow any concerns about the conduct or consequences of the work to be resolved"

MRC Guidance on Personal Information in Medical Research

<http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002452>

Any identifiable personal information such as the participant's name and address will however be destroyed at the end of the study period, using methods approved by Keele University, such as deletion of electronic records or shredding of paper records and subsequent disposal using the confidential waste system. This will ensure that personal data will not be stored for longer than is necessary (Data Protection Act 1998 (DPA) - Schedule 1, Part 1. *Research involving the NHS – retention of records*

<http://www.dh.gov.uk/en/Researchanddevelopment/AZ/Researchgovernance/index.htm>

The above information has been made explicit on page 2 of the Patient Information Sheet for the Questionnaires and the Focus group interview (version 2.0 dated 8th May 2012).

A section should be included in the Patient Information Sheet (questionnaires) about the risks of participating in the study. Information should be included in this section about the possibility of becoming distressed during the study and what should be done in this situation. Information should be included about support groups or charities that could be contacted if available

The nature of the questionnaire is not meant to be distressing, with anxiety and depression being assessed through validated questionnaires such as the PHQ9 in a target sample of participants with gout. However the small possibility of becoming distressed due to any of the questions has been made explicit in the Patient Information Sheet for the Questionnaires (The Gout Study Participant Information Sheet Version 2.0, dated 08/05/12). If a participant contacts us reporting that the questionnaires evoked unpleasant memories or thoughts which may appear to be a risk to either the participant themselves or others, we will inform the participant's General Practitioner (GP) as soon as possible. The participants will also be encouraged to contact their GP themselves should they feel distressed in any way as a consequence of completing the questionnaires. Taking on board the advice provided by the REC committee we have also included the contact details of NHS mental health support groups (relevant to the areas of participant recruitment) which do not require referral from a healthcare practitioner. All calls are free (call back also

available), confidential and support is provided by trained staff. For example, on average around 18000 calls per year are taken by the Staffordshire helpline and the team support approximately 60 potential suicide calls per month.

Mental Health Helpline Staffordshire (Brighter Futures)

0808 800 2234

Mental Health Helpline Shropshire

0800 195 1700

Mental Health Helpline Wolverhampton

0800 387034

The location of the interview should be given in the Patient Information Sheet (interviews).

The Gout Study Participant Information Sheet for Gout Interview Version 2.0 dated 08/05/12 has been updated with information regarding the location of the Focus group interviews either at the Arthritis Research UK Primary Care Centre or at the GP Surgery if appropriate.

It should be made clear in the Patient Information Sheet (interviews) that if distressed the participant could leave the interview.

The Gout Study Participant Information Sheet for Gout Interview Version 1.0 dated 15/02/12 states

“During the interview, you can choose not to answer questions, or to end the interview at any time, and for any reason. If an interview topic brings back unhappy memories or distressing thoughts that you do not wish to discuss, the topic will not be followed up again during the interview”

Following advice from the REC committee we have also added the following statement to clarify that by ending the interview the participant is also free to leave the place where the interview is being held;

“You will also be offered the option of leaving the place where the interview is being held should you wish to do so”.

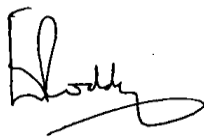
The contact details for someone who could be contacted in the event of distress should also be given at the end of the questionnaire.

Contact details of mental health helplines as listed previously have been added to the Gout Study Questionnaire booklets at baseline, 6 months, 12 months, 2 years and 3 Years (all Version 2.0 dated 08/05/12).

The Consent Form should include the following standard paragraph: 'I understand that my medical notes and data collected during the study may be looked at by individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to the records'.

The consent form at the end of 'The Gout Study - Baseline Questionnaire booklet Version 2.0, dated 08/05/12' has been updated with the above paragraph insertion.

Yours sincerely

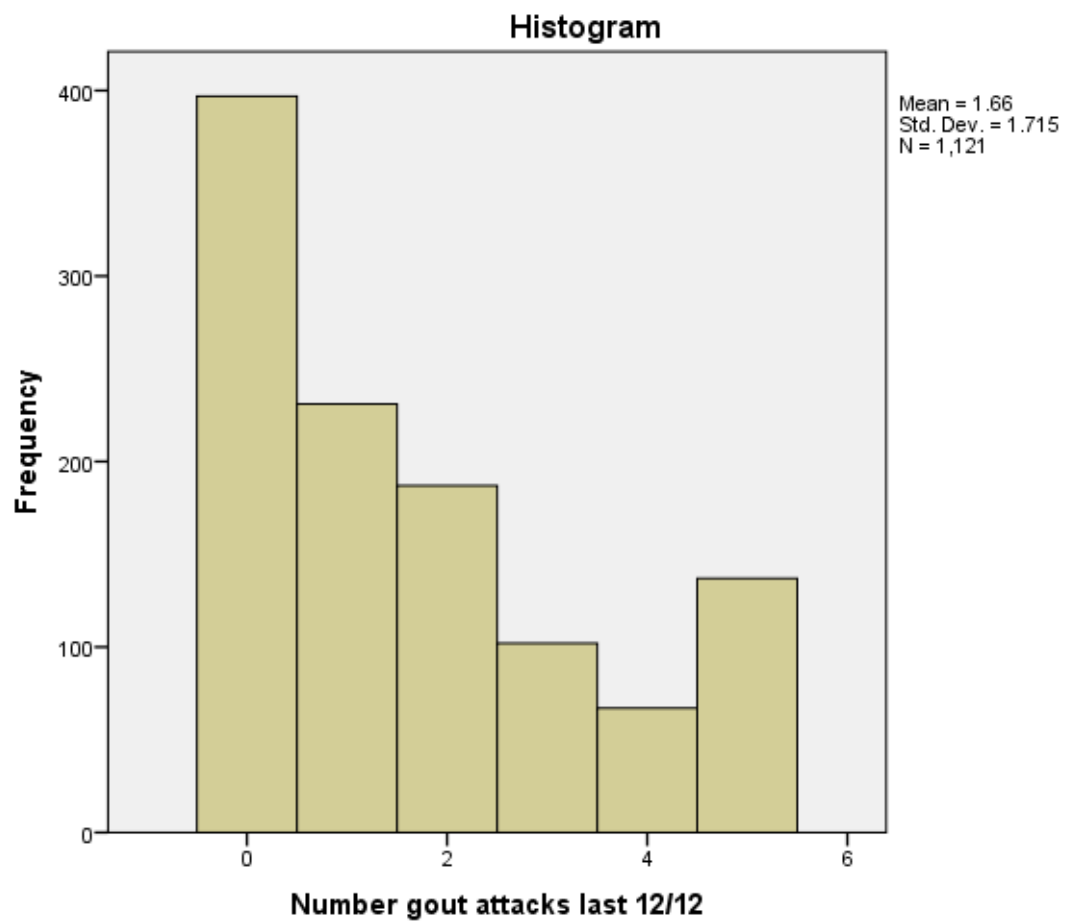


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Appendix 18: Testing for normal distribution of frequency of attacks data



Appendix 19: Graphical representation of tests for normal distribution of HRQOL measures

Figure 16

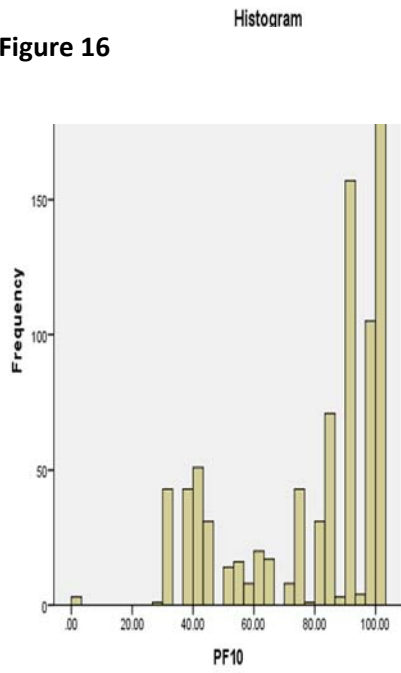


Figure 17

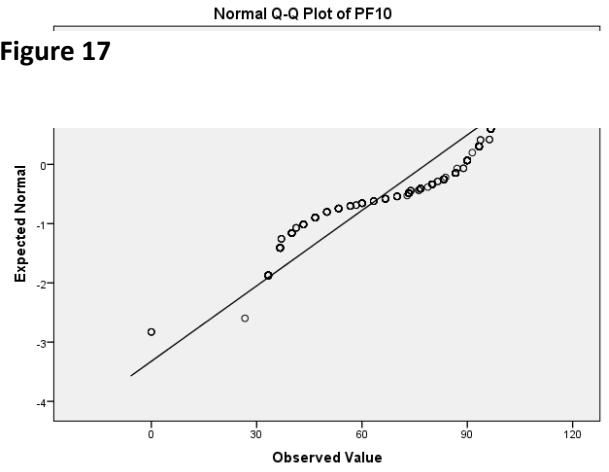


Figure 19

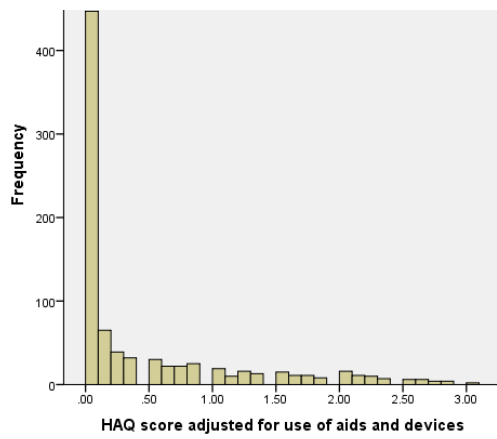


Figure 18

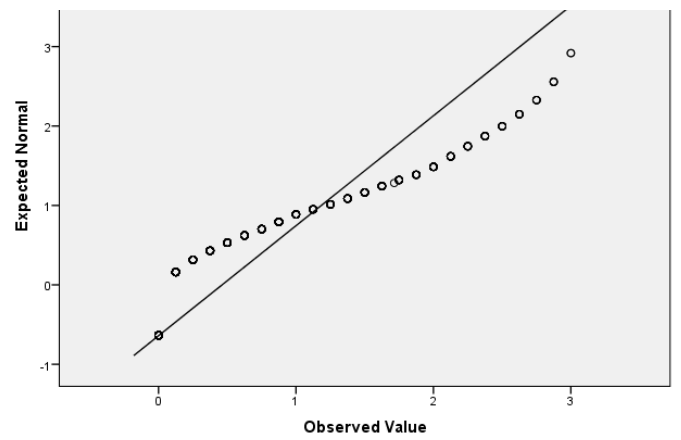


Figure 20

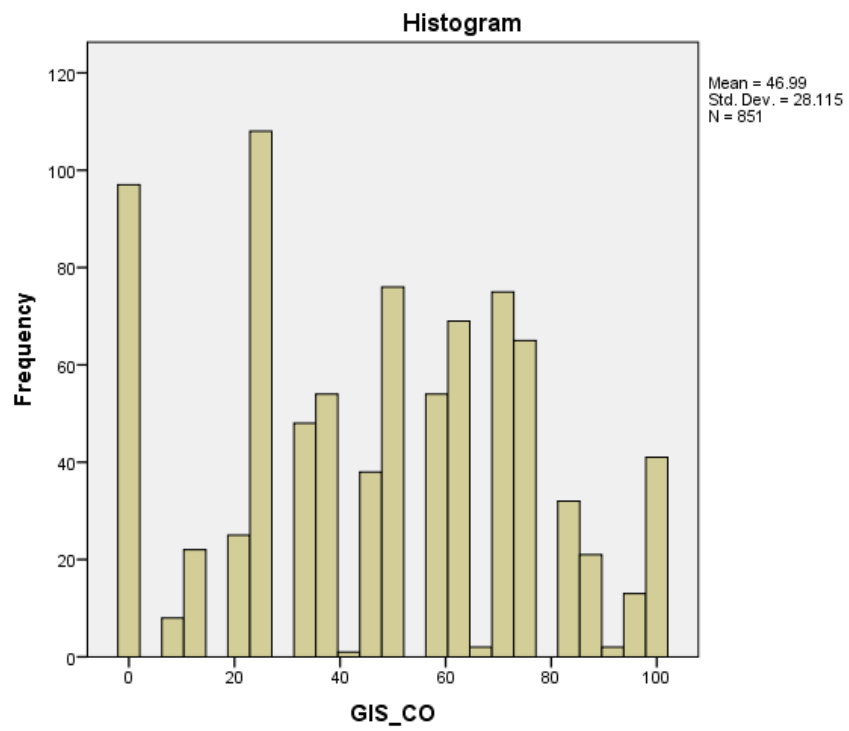


Figure 21

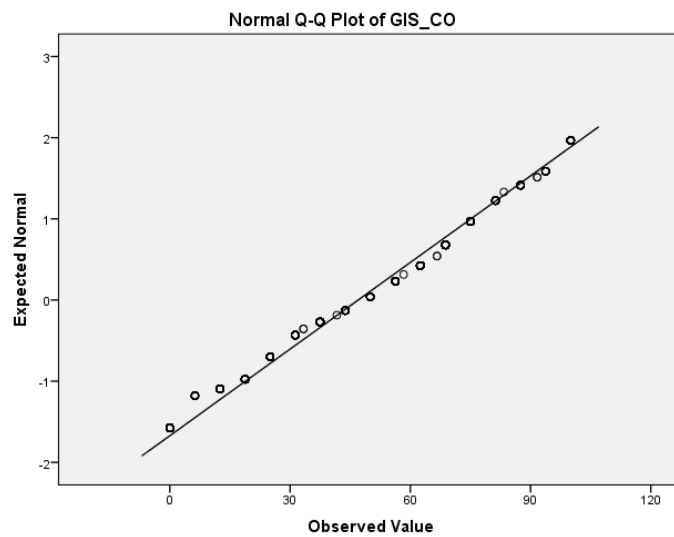


Figure 22

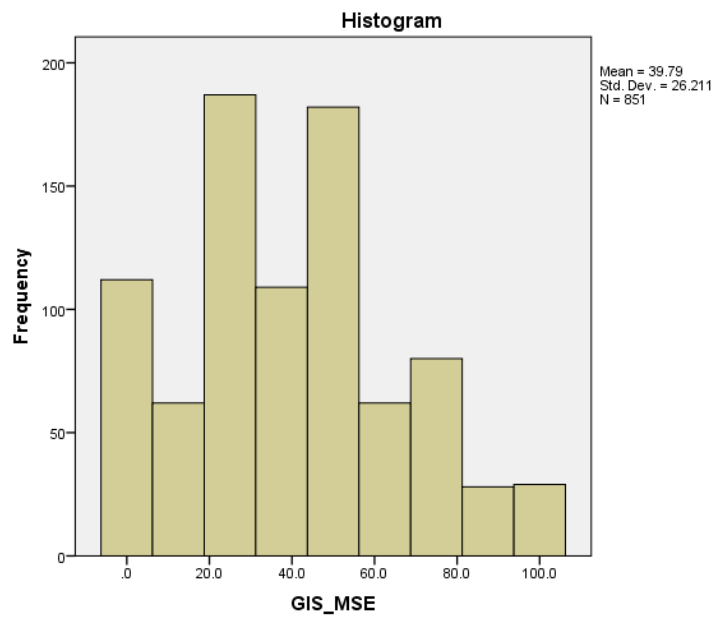


Figure 23

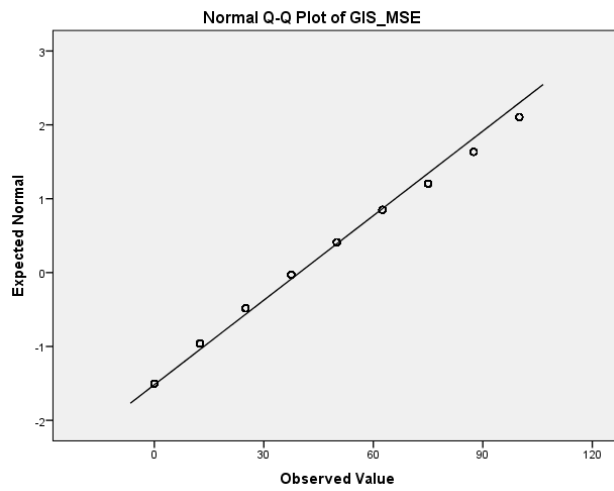


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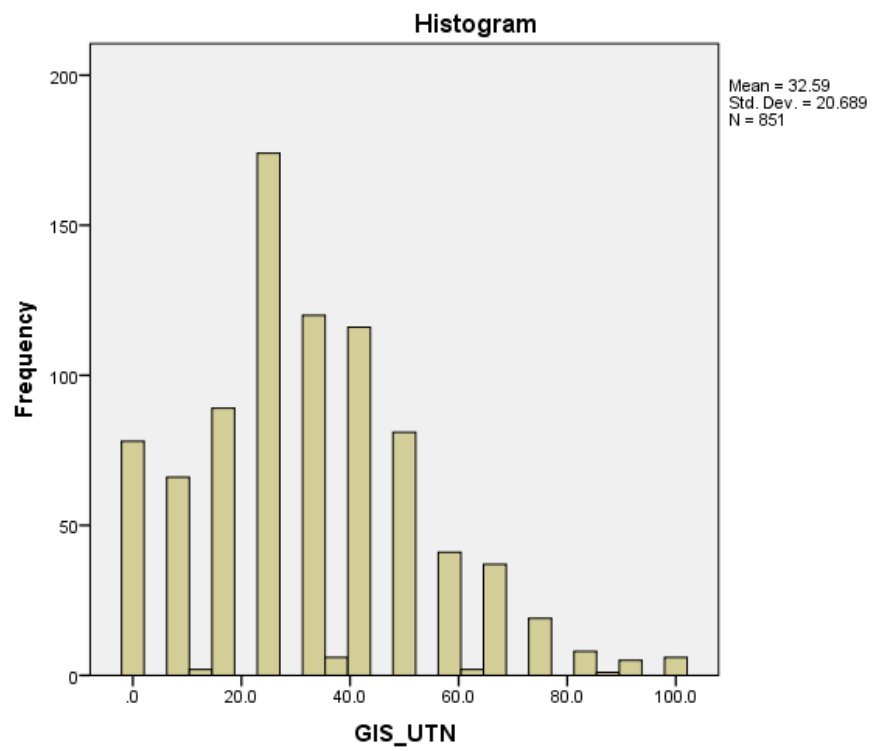


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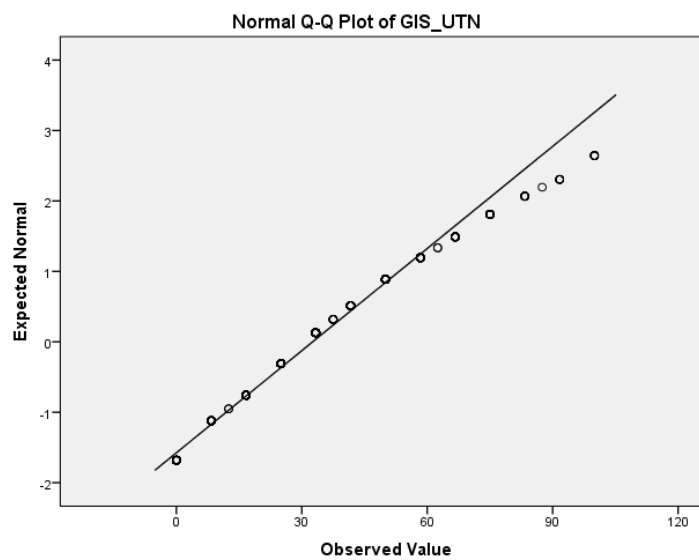


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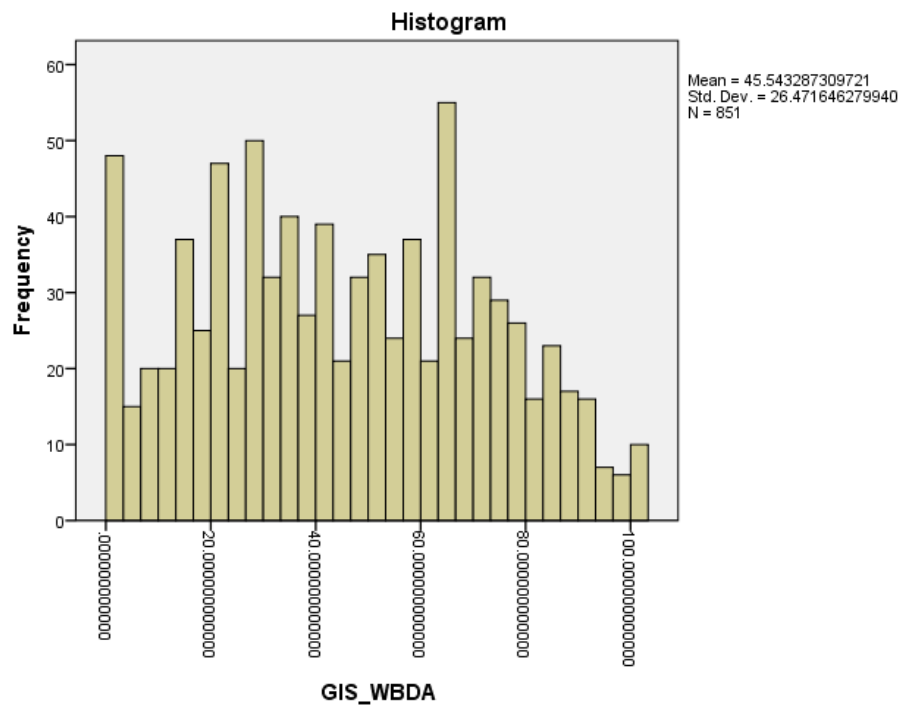


Figure 27

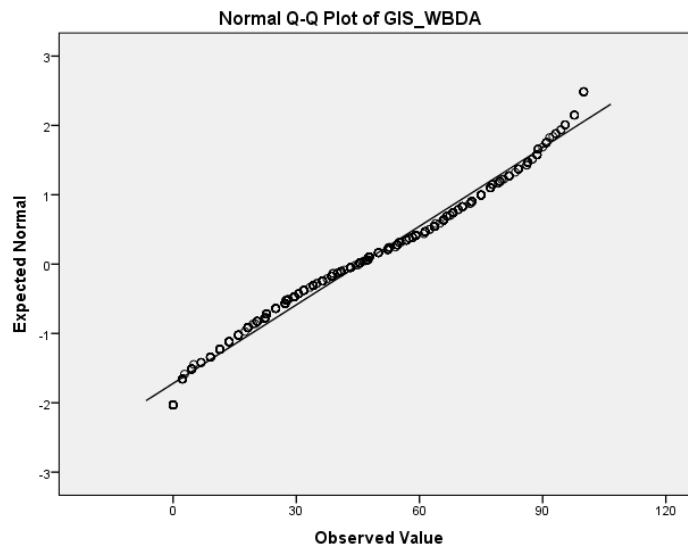


Figure 28

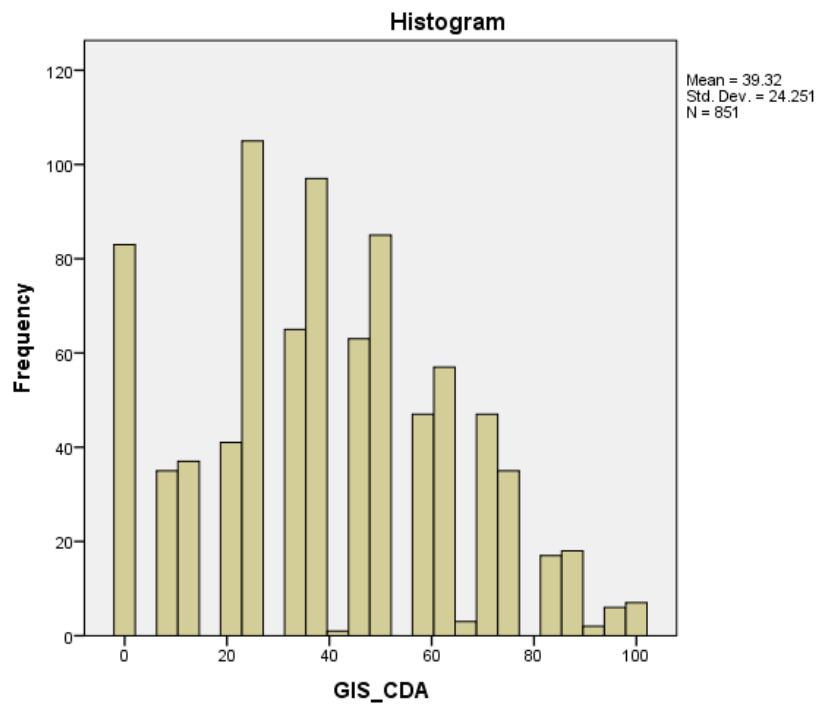


Figure 29

